

519	HSTBJ86	1466	Upregulation of CD152 and activation of T cells	<p>CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>Assays for the regulation of transcription through the FAS promoter element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the FAS promoter element in a reporter construct and to regulate transcription of FAS, a key enzyme for lipogenesis. FAS promoter is regulated by many transcription factors including SREBP. Insulin increases FAS gene transcription in livers of diabetic mice. This stimulation of transcription is also somewhat glucose dependent. Exemplary assays that may be used or routinely modified to test for FAS promoter element activity (in hepatocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Xiong, S., et al., Proc Natl Acad Sci U.S.A., 97(8):3948-53 (2000); Roder, K., et al.,</p>
520	HSUBW09	1467	Regulation of transcription through the FAS promoter element in hepatocytes	

520	HSUBW09	1467	Upregulation of CD152 and activation of T cells	<p>Eur J Biochem, 260(3):743-51 (1999); Oskouian B, et al., Biochem J, 317 (Pt 1):257-65 (1996); Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362-368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used according to these assays, such as H4IIE cells, are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays include rat liver hepatoma cell line(s) inducible with glucocorticoids, insulin, or cAMP derivatives.</p> <p>CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>IFNgamma FMAT. IFNγ plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNγ promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage</p>
521	HSVAM10	1468	Production of IFNgamma using a T cells	

522	HSVAT68	1469	<p>activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response development. Exemplary assays for transcription through the GATA3 response element that may be used or routinely modified to test GATA3-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA</p>

523	HSVBU91	1470	<p>85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p> <p>Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors that activate the cAMP signaling pathway. CREB plays a major role in adipogenesis, and is involved in differentiation into adipocytes. CRE contains the binding sequence for the transcription factor CREB (CRE binding protein). Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Reusch et al., Mol Cell Biol 20(3):1008-1020 (2000); and Klemm et al., J Biol Chem 273:917-923 (1998), the contents of each of which are herein incorporated by reference in its entirety. Pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p> <p>Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the</p>
523	HSVBU91	1470	<p>Activation of transcription through cAMP response element (CRE) in pre-adipocytes.</p> <p>Activation of Hepatocyte ERK Signaling Pathway</p>

523	HSVBU91	1470	Insulin Secretion	<p>invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Rat liver hepatoma cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat liver hepatoma cells that may be used according to these assays include H4Ile cells, which are known to respond to glucocorticoids, insulin, or cAMP derivatives.</p> <p>Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and dysregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); and, Miraglia S et al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated.</p> <p>Exemplary pancreatic cells that may be used according to these assays include HIT15 Cells. HIT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777</p> <p>Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.</p>
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523	HSV/BU91	1470	Activation of transcription through CD28 response element in immune cells (such as T-cells).	<p>Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.</p>
524	HSXCG83	1471	Production of IL-6	<p>IL-6 FMAAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these</p>

525	HSXEQ06	1472	Production of IL-2 and activation of T cells	<p>assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.</p> <p>IL-2 FMAT. IL-2 is the principal T cell factor that allows T cell expansion and differentiation into effector cells. Assays for immunomodulatory proteins secreted by TH1 cells that promote T cell and NK cell growth and differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, promote immune cell growth and differentiation, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-2, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Laduda et al., Immunology 94(4):496-502 (1998); and Powell et al., Immunol Rev 165:287-300 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors that activate the cAMP signaling pathway. CREB plays a major role in adipogenesis, and is involved in differentiation into adipocytes. CRE contains the binding sequence for the transcription factor CREB (CRE binding protein). Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test</p>
526	HSXGI47	1473	Activation of transcription through cAMP response element (CRE) in pre-adipocytes.	

526	HSXGI47	1473	Activation of Skeletal Muscle Cell PI3 Kinase Signalling Pathway	<p>cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Reusch et al., Mol Cell Biol 20(3):1008-1020 (2000); and Klemm et al., J Biol Chem 273:917-923 (1998), the contents of each of which are herein incorporated by reference in its entirety. Pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p> <p>Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose metabolism and cell survival are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein incorporated by reference in its entirety. Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat myoblast cells that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuses to form multinucleated myotubes and striated fibers after culture in differentiation media.</p>
527	HSYAV50	1474	Activation of transcription through cAMP response element (CRE) in pre-adipocytes.	<p>Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors that activate the cAMP</p>

527	HSYAV50	1474	<p>signaling pathway. CREB plays a major role in adipogenesis, and is involved in differentiation into adipocytes. CRE contains the binding sequence for the transcription factor CREB (CRE binding protein). Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Reusch et al., Mol Cell Biol 20(3):1008-1020 (2000); and Klemm et al., J Biol Chem 273:917-923 (1998), the contents of each of which are herein incorporated by reference in its entirety. Pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p> <p>Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).</p>
527	HSYAV50	1474	<p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the</p>

528	HSYAV66	1475	Production of IL-6	<p>invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.</p> <p>IL-6 FMAAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when</p>
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529	HSYAZ50	1476	Activation of transcription through NFKB response element in immune cells (such as T-cells).	activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.
530	HSYAZ63	1477	Activation of Adipocyte PI3 Kinase Signalling Pathway	Kinase assay. Kinase assays, for example an GSK-3 assays, for PI3 kinase signal transduction that regulate glucose metabolism and cell survival are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.
530	HSYAZ63	1477	Activation of	Assays for the activation of transcription through the Gamma Interferon Activation Site

			transcription through GAS response element in immune cells (such as T-cells).	(GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Hentinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).
531	HSYBG37	1478	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.
531	HSYBG37	1478	Activation of JNK Signaling Pathway in	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely

			immune cells (such as eosinophils).	<p>modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction. Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.</p>
532	HSZAF47	1479	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).	<p>Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et</p>

				<p>al., <i>Exp Cell Res</i> 247(2): 495-504 (1999); Kyriakis JM, <i>Biochem Soc Symp</i> 64:29-48 (1999); Chang and Karin, <i>Nature</i> 410(6824):37-40 (2001); and Cobb MH, <i>Prog Biophys Mol Biol</i> 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction. Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" <i>Clin Exp Immunol</i>; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" <i>J Exp Med</i>; Feb 2;187(3):415-25 (1998); <i>J Allergy Clin Immunol</i> 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" <i>J Allergy Clin Immunol</i>; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.</p>
533	HT3SF53	1480	Production of IL-6	<p>IL-6 FMA T. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention</p>

534	HT5GJ57	1481	Activation of transcription through AP1 response element in immune cells (such as T-cells).	<p>(including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.</p> <p>Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.</p> <p>MCP-1 FMA.T. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation. Exemplary assays that test for immunomodulatory proteins evaluate the production of cell surface markers, such as monocyte chemoattractant protein (MCP), and the activation of monocytes and T cells. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include</p>
534	HT5GJ57	1481	Production of MCP-1	

535	HTADW91	1482	Activation of Hepatocyte ERK Signaling Pathway	<p>assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Sathaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.</p> <p>Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Rat liver hepatoma cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat liver hepatoma cells that may be used according to these assays include H4Ile cells, which are known to respond to glucocorticoids, insulin, or cAMP derivatives.</p>
536	HTADX17	1483	Activation of transcription through NFAT response in immune cells (such as T-cells).	<p>Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346</p>

536	HTADX17	1483	<p>Activation of transcription through GAS response element in immune cells (such as T-cells).</p>	<p>(1988); Serfling et al., <i>Biochim Biophys Acta</i> 1498(1):1-18 (2000); De Boer et al., <i>Int J Biochem Cell Biol</i> 31(10):1221-1236 (1999); Fraser et al., <i>Eur J Immunol</i> 29(3):838-844 (1999); and Yeseen et al., <i>J Biol Chem</i> 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.</p> <p>Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., <i>Gene</i> 66:1-10 (1998); Cullen and Malm, <i>Methods in Enzymol</i> 216:362-368 (1992); Henthorn et al., <i>Proc Natl Acad Sci USA</i> 85:6342-6346 (1988); Matikainen et al., <i>Blood</i> 93(6):1980-1991 (1999); and Hentinen et al., <i>J Immunol</i> 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4 cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).</p>
536	HTADX17	1483	<p>Activation of transcription through NFKB response element in immune cells (such as T-cells).</p>	<p>Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., <i>Gene</i> 66:1-10 (1998); Cullen and Malm, <i>Methods in Enzymol</i> 216:362-368 (1992); Henthorn et al., <i>Proc Natl Acad Sci USA</i> 85:6342-6346 (1988); Black et al., <i>Virus Gnes</i> 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are</p>

537	HTAEE28	1484	Protection from Endothelial Cell Apoptosis.	<p>herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).</p> <p>Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess the ability of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to inhibit caspase protease-mediated apoptosis. Exemplary assays for caspase apoptosis that may be used or routinely modified to test caspase apoptosis rescue of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Romeo et al., <i>Cardiovasc Res</i> 45(3): 788-794 (2000); Messmer et al., <i>Br J Pharmacol</i> 127(7): 1633-1640 (1999); and <i>J Atheroscler Thromb</i> 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary endothelial cells that may be used according to these assays include bovine aortic endothelial cells (bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.</p>
537	HTAEE28	1484	Insulin Secretion	<p>Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and dysregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., <i>Endocr J</i>, 47(3):261-9 (2000); Salapatek, A.M., et al., <i>Mol Endocrinol</i>, 13(8):1305-17 (1999); Filipsson, K., et al., <i>Ann N Y Acad Sci</i>, 865:441-4 (1998); Olson, L.K., et al., <i>J Biol Chem</i>, 271(28):16544-52 (1996); and, Miraglia S et al., <i>Journal of Biomolecular Screening</i>, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HTT15</p>

538	HTDAF28	1485	Activation of Adipocyte ERK Signaling Pathway	<p>Cells. HTT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777</p> <p>Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.</p>
538	HTDAF28	1485	Upregulation of HLA-DR and activation of T cells	<p>Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p> <p>HLA-DR FMAT. MHC class II is essential for correct presentation of antigen to CD4+ T cells. Deregulation of MHC class II has been associated with autoimmune diseases (e.g., diabetes, rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis). Assays for immunomodulatory proteins expressed on MHC class II expressing T cells and antigen presenting cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of MHC class II products, such as HLA-DR antigens, and the activation of T cells. Such assays</p>

538	HTDAF28	1485	Upregulation of CD69 and activation of T cells	<p>that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Lamour et al., Clin Exp Immunol 89(2):217-222 (1992); Hurme and Sihvola, Immunol Lett 20(3):217-222 (1989); Gansbacher and Zier, Cell Immunol 117(1):22-34 (1988); and Itoh et al., J Histochem Cytochem 40(11):1675-1683, the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>CD69 FMAT. CD69 is an activation marker that is expressed on activated T cells, B cells, and NK cells. CD69 is not expressed on resting T cells, B cells, or NK cells. CD69 has been found to be associated with inflammation. Assays for immunomodulatory proteins expressed in T cells, B cells, and leukocytes are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD69, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Ferenczi et al., J Autoimmun 14(1):63-78 (2000); Werfel et al., Allergy 52(4):465-469 (1997); Taylor-Fishwick and Siegel, Eur J Immunol 25(12):3215-3221 (1995); and Afetra et al., Ann Rheum Dis 52(6):457-460 (1993), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and</p>
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538	HTDAF28	1485	Upregulation of CD152 and activation of T cells	<p>may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346</p>
539	HTDAF65	1486	Activation of transcription through STAT6 response element in immune cells (such as T-cells).	

540	HTEBI28	1487	Production of IL-5	<p>(1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur J Immunol 27(8):1982-1987 (1997); and Masuda et al., J Biol Chem 275(38):29331-29337 (2000), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.</p> <p>IL-5 FMA T. Assays for immunomodulatory proteins secreted by TH2 cells, mast cells, basophils, and eosinophils that stimulate eosinophil function and B cell Ig production and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cell function, modulate B cell Ig production, modulate immune cell polarization, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-5, and the stimulation of eosinophil function and B cell Ig production. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Ohshima et al., Blood 92(9):3338-3345 (1998); Jung et al., Eur J Immunol 25(8):2413-2416 (1995); Mori et al., J Allergy Clin Immunol 106(1 Pt 2):558-564 (2000); and Koning et al., Cytokine 9(6):427-436 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p>
540	HTEBI28	1487	Upregulation of CD71 and activation of T cells	<p>CD71 FMA T. CD71 is the transferrin receptor. Transferrin is a major iron carrying protein that is essential for cell proliferation. CD71 is expressed predominantly on cells that are actively proliferating. Assays for immunomodulatory proteins expressed on activated T cells, B cells, and most proliferating cells are well known in the art and</p>

541	HTEDF80	1488	Upregulation of CD152 and activation of T cells	<p>may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD71, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Afetra et al., Ann Rheum Dis 52(6):457-460 (1993), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its</p>
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542	HTEDY42	1489	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	<p>entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response development. Exemplary assays for transcription through the GATA3 response element that may be used or routinely modified to test GATA3-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p>
542	HTEDY42	1489	Upregulation of CD154 and activation of T cells	<p>CD154 FMAT. CD154 (a.k.a., CD40L) expression is induced following activation of T cells. Interaction between CD154 and CD40 on B cells is required for correct antibody class switching and germinal center formation. Mutations in CD154 are linked to immunodeficiencies and increased susceptibility to infections. Assays for immunomodulatory proteins important for antibody class switching and TH1 function and expressed on activated T helper lymphocytes are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the</p>

543	HTEFU65	1490	<p>activation of T cells, modulate antibody class switching, mediate TH1 function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD154, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Mackey et al., J Leukoc Biol 63(4):418-428 (1998); and Skov et al., 164(7):3500-3505 (2000), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors that activate the cAMP signaling pathway. CREB plays a major role in adipogenesis, and is involved in differentiation into adipocytes. CRE contains the binding sequence for the transcription factor CREB (CRE binding protein). Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Reusch et al., Mol Cell Biol 20(3):1008-1020 (2000); and Klemm et al., J Biol Chem 273:917-923 (1998), the contents of each of which are herein incorporated by reference in its entirety. Pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte</p>
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543	HTEFU65	1490	Regulation of Malic Enzyme in hepatocytes	<p>cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p> <p>Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesis and its expression is stimulated by insulin. ME promoter contains two direct repeat (DR1)-like elements MEp and MED identified as putative PPAR response elements. ME promoter may also respond to AP1 and other transcription factors. Exemplary assays that may be used or routinely modified to test for regulation of transcription of Malic Enzyme (in hepatocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Streeter, R.S., et al., <i>Mol Endocrinol</i>, 12(11):1778-91 (1998); Garcia-Jimenez, C., et al., <i>Mol Endocrinol</i>, 8(10):1361-9 (1994); Barroso, I., et al., <i>J Biol Chem</i>, 274(25):17997-8004 (1999); Ijpenberg, A., et al., <i>J Biol Chem</i>, 272(32):20108-20117 (1997); Berger, et al., <i>Gene</i> 66:1-10 (1988); and, Cullen, B., et al., <i>Methods in Enzymol.</i> 216:362-368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays include the mouse 3T3-L1 cell line. 3T3-L1 is a mouse preadipocyte cell line (adherent). It is a continuous substrain of 3T3 fibroblasts developed through clonal isolation. Cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.</p>
543	HTEFU65	1490	Myoblast cell proliferation	<p>Assays for muscle cell proliferation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit myoblast cell proliferation. Exemplary assays for myoblast cell proliferation that may be used or routinely modified to test activity of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) include, for example, assays disclosed in: Soeta, C., et al. "Possible role for the c-ski gene in the proliferation of myogenic cells in regenerating skeletal muscles of rats" <i>Dev Growth Differ</i></p>

543	HTEFU65	1490	Production of IFN γ using a T cells	<p>Apr;43(2):155-64 (2001); Ewton DZ, et al., "IGF binding proteins-4, -5 and -6 may play specialized roles during L6 myoblast proliferation and differentiation" J Endocrinol Mar;144(3):539-53 (1995); and, Pampusch MS, et al., "Effect of transforming growth factor beta on proliferation of L6 and embryonic porcine myogenic cells" J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.</p> <p>IFNγ plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNγ promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNγ), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to</p>
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543	HTEFU65	1490	Stimulation of insulin secretion from pancreatic beta cells.	<p>immunomodulatory factors.</p> <p>Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and dysregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., <i>Am J Physiol</i>, 277(4 Pt 2):R959-66 (1999); Li, M., et al., <i>Endocrinology</i>, 138(9):3735-40 (1997); Kim, K.H., et al., <i>FEBS Lett</i>, 377(2):237-9 (1995); and, Miraglia S et al., <i>Journal of Biomolecular Screening</i>, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. <i>Endocrinology</i> 1992 130:167.</p>
544	HTEGA76	1491	Activation of Adipocyte ERK Signaling Pathway	<p>Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., <i>Biol Chem</i> 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, <i>Exp Clin Endocrinol Diabetes</i> 107(2):126-132 (1999); Kyriakis JM, <i>Biochem Soc Symp</i> 64:29-48 (1999); Chang and Karin, <i>Nature</i> 410(6824):37-40 (2001); and Cobb MH, <i>Prog Biophys Mol Biol</i> 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that</p>

544	HTEGA76	1491	Endothelial Cell Apoptosis	<p>may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p> <p>Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test caspase apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary endothelial cells that may be used according to these assays include bovine aortic endothelial cells (bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.</p>
545	HTEGI42	1492	Activation of transcription through NFAT response in immune cells (such as T-cells).	<p>Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Serfling et al., Biochim Biophys Acta 1498(1):1-18 (2000); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents</p>

546	HTEHR24	1493	Production of IL-4	<p>of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.</p> <p>IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cells, modulate immune cell polarization, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1994); Yssel et al., Res Immunol 144(8):610-616 (1993); Bagley et al., Nat Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and</p>
546	HTEHR24	1493	Upregulation of CD152 and activation of T cells	

547	HTEHU93	1494	<p>agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to</p>
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547	HTEHU93	1494	Production of IL-10 and activation of T-cells.	<p>these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p> <p>Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) to modulate IL-10 production and/or T-cell proliferation include, for example, assays such as disclosed and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease" Br Med Bull; 56 (4): 956-968 (2000), and Cohn, et al., "T-helper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.</p> <p>Assays for the activation of transcription through the NFkB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFkB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFkB response element that may be used or routinely modified to test NFkB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).</p>
548	HTEIP36	1495	Activation of transcription through NFkB response element in immune cells (such as T-cells).	

548	HTEIP36	1495	Production of IL-10 and activation of T-cells.	<p>Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) to modulate IL-10 production and/or T-cell proliferation include, for example, assays such as disclosed and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease" Br Med Bull; 56 (4): 956-968 (2000), and Cohn, et al., "T-helper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.</p> <p>Assays for the activation of transcription through the NFkB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFkB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFkB response element that may be used or routinely modified to test NFkB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).</p>
549	HTEIV80	1496	Activation of transcription through NFkB response element in immune cells (such as T-cells).	<p>Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the</p>
550	HTEIN13	1497	Activation of Adipocyte ERK Signaling Pathway	

550	HTEJN13	1497	Upregulation of CD69 and activation of T cells	<p>invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., <i>Biol Chem</i> 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, <i>Exp Clin Endocrinol Diabetes</i> 107(2):126-132 (1999); Kyriakis JM, <i>Biochem Soc Symp</i> 64:29-48 (1999); Chang and Karin, <i>Nature</i> 410(6824):37-40 (2001); and Cobb MH, <i>Prog Biophys Mol Biol</i> 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p> <p>CD69 FMAT. CD69 is an activation marker that is expressed on activated T cells, B cells, and NK cells. CD69 is not expressed on resting T cells, B cells, or NK cells. CD69 has been found to be associated with inflammation. Assays for immunomodulatory proteins expressed in T cells, B cells, and leukocytes are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD69, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., <i>J Biomolecular Screening</i> 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Ferenczi et al., <i>J Autoimmun</i> 14(1):63-78 (2000); Werfel et al., <i>Allergy</i> 52(4):465-469 (1997); Taylor-Fishwick and Siegel, <i>Eur J Immunol</i> 25(12):3215-3221 (1995); and Afetra et al., <i>Ann Rheum Dis</i> 52(6):457-460 (1993), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are</p>
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551	HTELM16	1498	Production of MIP1alpha	<p>primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>MIP-1alpha FMT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Sathaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.</p> <p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117</p>
551	HTELM16	1498	Activation of transcription through serum response element in immune cells (such as T-cells).	

552	HTEPG70	1499	<p>Activation of transcription through cAMP response element (CRE) in pre-adipocytes.</p>	<p>(1997), the content of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.</p> <p>Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors that activate the cAMP signaling pathway. CREB plays a major role in adipogenesis, and is involved in differentiation into adipocytes. CRE contains the binding sequence for the transcription factor CREB (CRE binding protein). Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Reusch et al., Mol Cell Biol 20(3):1008-1020 (2000); and Klemm et al., J Biol Chem 273:917-923 (1998), the contents of each of which are herein incorporated by reference in its entirety. Pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p> <p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays</p>
552	HTEPG70	1499	<p>Activation of transcription through serum response element in pre-adipocytes.</p>	

552	HTEPG70	1499	<p>disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. Pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p> <p>This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response development. Exemplary assays for transcription through the GATA3 response element that may be used or routinely modified to test GATA3-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p>
552	HTEPG70	1499	<p>Activation of transcription through GATA-3 response element in immune cells (such as mast cells).</p> <p>Activation of transcription through NFAT response</p>

			<p>Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p>
552	HTEPG70	1499	<p>Activation of transcription through NFkB response element in immune cells (such as basophils).</p> <p>This reporter assay measures activation of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation of transcription through the NFkB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFkB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFkB response element that may be used or routinely modified to test NFkB-agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Marone et al., Int Arch Allergy Immunol 114(3):207-17 (1997), the contents of each of which are herein incorporated by reference in its entirety. Basophils that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human basophil cell lines that may be used according to these assays include Ku812, originally established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line</p>

552	HTEPG70	1499	Activation of transcription through NFKB response element in immune cells (such as T-cells).	<p>that can be induced to differentiate into mature basophils.</p> <p>Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.</p> <p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.</p>
552	HTEPG70	1499	Activation of transcription through serum response element in immune cells (such as natural killer cells).	
553	HTGAU75	1500	Upregulation of CD71 and activation of T	<p>CD71 FMA7. CD71 is the transferrin receptor. Transferrin is a major iron carrying protein that is essential for cell proliferation. CD71 is expressed predominantly on</p>

554	HTGEP89	1501	cells	<p>cells that are actively proliferating. Assays for immunomodulatory proteins expressed on activated T cells, B cells, and most proliferating cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD71, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Afetra et al., Ann Rheum Dis 52(6):457-460 (1993), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.</p> <p>Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and</p>
555	HTHBG43	1502	Activation of transcription through	<p>Activation of transcription through serum response element in immune cells (such as T-cells).</p> <p>Activation of transcription through</p>

555	HTHBG43	1502	STAT6 response element in immune cells (such as T-cells).	<p>may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur J Immunol 27(8):1982-1987 (1997); and Masuda et al., J Biol Chem 275(38):29331-29337 (2000), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.</p> <p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.</p>
556	HTHCA18	1503	Production of GM-CSF	<p>GM-CSF FMA T. GM-CSF is expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytes- macrophage progenitors and enhances antimicrobial activity in</p>

				<p>neutrophils, monocytes and macrophage. Additionally, GM-CSF plays an important role in the differentiation of dendritic cells and monocytes, and increases antigen presentation. GM-CSF is considered to be a proinflammatory cytokine. Assays for immunomodulatory proteins that promote the production of GM-CSF are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and modulate the growth and differentiation of leukocytes. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as GM-CSF, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Ye et al., J Leukoc Biol (58(2):225-233, the contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC) or may be isolated using techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.</p>
557	HTHDJ94	1504	Production of IL-6	<p>IL-6 FMAAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test</p>

558	HTHDS25	1505	<p>immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.</p> <p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.</p> <p>Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors that activate the cAMP signaling pathway. CREB plays a major role in adipogenesis, and is involved in differentiation into adipocytes. CRE contains the binding sequence for the transcription factor CREB (CRE binding protein). Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test</p>
559	HTJMA95	1506	<p>Activation of transcription through serum response element in immune cells (such as T-cells).</p> <p>Activation of transcription through cAMP response element (CRE) in pre-adipocytes.</p>

559	HTJMA95	1506	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).	<p>cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Reusch et al., Mol Cell Biol 20(3):1008-1020 (2000); and Klemm et al., J Biol Chem 273:917-923 (1998), the contents of each of which are herein incorporated by reference in its entirety. Pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p> <p>Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction. Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils"</p>
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559	HTJMA95	1506	Activation of transcription through API response element in immune cells (such as T-cells).	<p>J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.</p> <p>Assays for the activation of transcription through the API response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the API response element that may be used or routinely modified to test API-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is an IL-2 and IL-4 responsive suspension-culture cell line.</p>
559	HTJMA95	1506	Activation of transcription through CD28 response element in immune cells (such as T-cells).	<p>Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 273(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to</p>

559	HTJMA95	1506	Activation of transcription through NFAT response element in immune cells (such as T-cells).	<p>these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.</p> <p>Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Serfling et al., Biochim Biophys Acta 1498(1):1-18 (2000); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.</p>
559	HTJMA95	1506	Activation of transcription through NFKB response element in immune cells (such as T-cells).	<p>Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a</p>

559	HTJMA95	1506	Production of IL-10 and activation of T-cells.	<p>suspension culture of IL-2 and IL-4 responsive T cells.</p> <p>Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) to modulate IL-10 production and/or T-cell proliferation include, for example, assays such as disclosed and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease" Br Med Bull; 56 (4): 956-968 (2000), and Cohn, et al., "T-helper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.</p>
560	HTJML75	1507	Production of GM-CSF	<p>GM-CSF FMAAT. GM-CSF is expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytes- macrophage progenitors and enhances antimicrobial activity in neutrophils, monocytes and macrophage. Additionally, GM-CSF plays an important role in the differentiation of dendritic cells and monocytes, and increases antigen presentation. GM-CSF is considered to be a proinflammatory cytokine. Assays for immunomodulatory proteins that promote the production of GM-CSF are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and modulate the growth and differentiation of leukocytes. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as GM-CSF, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and</p>

561	HTLAA40	1508	<p>Activation of transcription through GATA-3 response element in immune cells (such as mast cells).</p>	<p>Ye et al., J Leukoc Biol (58(2):225-233, the contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC) or may be isolated using techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.</p> <p>This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response development. Exemplary assays for transcription through the GATA3 response element that may be used or routinely modified to test GATA3-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p> <p>Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response</p>
562	HTLBE23	1509	<p>Activation of transcription through AP1 response element in immune cells (such as T-cells).</p>	

563	HTLEP53	1510	Endothelial Cell Apoptosis	<p>element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.</p> <p>Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test caspase apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary endothelial cells that may be used according to these assays include bovine aortic endothelial cells (bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.</p> <p>Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and dysregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion</p>
563	HTLEP53	1510	Insulin Secretion	

564	HTLFE42	1511	<p>(from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., <i>Endocr J</i>, 47(3):261-9 (2000); Salapatek, A.M., et al., <i>Mol Endocrinol</i>, 13(8):1305-17 (1999); Filipsson, K., et al., <i>Ann N Y Acad Sci</i>, 865:441-4 (1998); Olson, L.K., et al., <i>J Biol Chem</i>, 271(28):16544-52 (1996); and, Miraglia S et al., <i>Journal of Biomolecular Screening</i>, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HIT15 Cells. HIT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATCC# CRL-1777</p> <p>Refs: Lord and Ashcroft. <i>Biochem. J</i>. 219: 547-551; Santerre et al. <i>Proc. Natl. Acad. Sci. USA</i> 78: 4339-4343, 1981.</p>
565	HTLFE57	1512	<p>Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., <i>Gene</i> 66:1-10 (1998); Cullen and Malm, <i>Methods in Enzymol</i> 216:362-368 (1992); Henthorn et al., <i>Proc Natl Acad Sci USA</i> 85:6342-6346 (1988); Georas et al., <i>Blood</i> 92(12):4529-4538 (1998); Moffatt et al., <i>Transplantation</i> 69(7):1521-1523 (2000); Curiel et al., <i>Eur J Immunol</i> 27(8):1982-1987 (1997); and Masuda et al., <i>J Biol Chem</i> 275(38):29331-29337 (2000), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.</p>
			<p>Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention</p>

				(including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).
566	HTLGE31	1513	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.
567	HTLHY14	1514	Calcium flux in immune cells (such as monocytes)	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux in immune cells (such as monocytes) include assays disclosed in: Chan, CC, et al., J Pharmacol Exp Ther, 269(3):891-896 (1994); Andersson, K, et al., Cytokine, 12(12):1784-1787 (2000); Scully, SP, et al., J Clin Invest, 74(2) 589-599 (1984); and, Sullivan, E, et al., Methods Mol Biol, 114:125-133 (1999), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used

568	HTLIT32	1515	Production of IL-4	<p>according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the THP-1 monocyte cell line.</p> <p>IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cells, modulate immune cell polarization, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1994); Yssel et al., Res Immunol 144(8):610-616 (1993); Bagley et al., Nat Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in</p>
569	HTLIV19	1516	Activation of transcription through STAT6 response element in immune cells (such as natural killer cells).	

569	HTLV19	1516	<p>Activation of transcription through NFAT response element in immune cells (such as natural killer cells).</p>	<p>Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur J Immunol 27(8):1982-1987 (1997); and Masuda et al., J Biol Chem 275(38):29331-29337 (2000), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC).</p> <p>Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.</p>
569	HTLV19	1516	<p>Activation of transcription through serum response element in immune cells (such as natural killer cells).</p>	<p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in</p>

570	HTNBO91	1517	Production of ICAM-1	<p>Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.</p> <p>Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.</p>
571	HTOAK16	1518	Activation of transcription through serum response element in immune cells (such as T-cells).	<p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.</p>

571	HTOAK16	1518	<p>Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))</p>	<p>Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to measure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.</p>
571	HTOAK16	1518	<p>Production of IL-8 by endothelial cells (such as Human Umbilical Cord Endothelial Cells).</p>	<p>Assays measuring production of IL-8 are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate production and/or secretion of IL-8. For example, FMAT may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate production and/or secretion of IL-8 from endothelial cells (such as human umbilical vein endothelial cells (HUVEC)). HUVECs are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Endothelial cells play a pivotal role in the initiation and perpetuation of inflammation and secretion of IL-8 may play an important role in recruitment and activation of immune cells such as neutrophils, macrophages, and lymphocytes.</p>
571	HTOAK16	1518	<p>Production of ICAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))</p>	<p>Endothelial cells, which are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used in ICAM production assays include human umbilical vein endothelial cells (HUVEC), and are available from commercial sources. The expression of ICAM (CD54),^a integral membrane protein, can be upregulated by cytokines or other factors, and ICAM expression is important in mediating immune and endothelial cell interactions leading to immune and inflammatory responses. Assays for measuring expression of</p>

571	HTOAK16	1518	Production of IL-13	<p>ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety.</p> <p>IL-13 FMA.T. IL-13 enhances IgM, IgG, and IgE production and induces FcER1. IL-13 has anti-inflammatory activity on monocytes and macrophages. Assays for immunomodulatory proteins produced by T cells that inhibit activation and release of cytokines by macrophages are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate cytokine release, stimulate immune cells through the binding of IL-13 and IL-4 receptors, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-13, the inhibition of cytokines released by macrophages. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Ohshima et al., Blood 92(9):3338-3345 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary</p>
572	HTODK73	1519	Activation of transcription through NFAT response in immune cells (such as T-cells).	

573	HTOD072	1520	Upregulation of CD152 and activation of T cells	<p>assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Serfling et al., Biochim Biophys Acta 1498(1):1-18 (2000); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.</p> <p>CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor</p>
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574	HTOGR42	1521	Activation of transcription through serum response element in immune cells (such as T-cells).	and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.
574	HTOGR42	1521	Activation of Endothelial Cell JNK Signaling Pathway.	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.
574	HTOGR42	1521	Activation of Natural	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal

575	HTOHM15	1522	Killer Cell ERK Signaling Pathway.	transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary natural killer cells that may be used according to these assays include the human natural killer cell lines (for example, NK-YT cells which have cytolytic and cytotoxic activity) or primary NK cells.
			Activation of JNK Signaling Pathway in immune cells (such as eosinophils).	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction. Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced

576	HTOHT18	1523	Activation of transcription through serum response element in immune cells (such as T-cells).	<p>apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct; 122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2; 187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep; 104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep; 104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.</p> <p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.</p>
576	HTOHT18	1523	Production of TNF alpha by dendritic cells	<p>TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays</p>

577	HTOIY21	1524	Activation of Skeletal Muscle Cell ERK Signalling Pathway	<p>disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1998); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.</p> <p>Kinase assay. Kinase assays, for examplek Elk-1 kinase assays, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat myoblast cells that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuses to form multinucleated myotubes and striated fibers after culture in differentiation media.</p> <p>Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test caspase apoptosis activity of polypeptides of the invention (including</p>
578	HTOIZ02	1525	Endothelial Cell Apoptosis	

578	HTOIZ02	1525	Production of IL-6	<p>antibodies and agonists or antagonists of the invention) include the assays disclosed in Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary endothelial cells that may be used according to these assays include bovine aortic endothelial cells (bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.</p> <p>IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.</p>
579	HTOJA73	1526	Production of	IFNgamma FMAT. IFNγ plays a central role in the immune system and is considered

			IFN γ using a T cells	<p>to be a proinflammatory cytokine. IFNγ promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNγ), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p>
580	HTOJK60	1527	Activation of transcription through serum response element in immune cells (such as T-cells).	<p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of</p>

581	HTPBW79	1528	Activation of transcription through NFAT response element in immune cells (such as mast cells).	<p>which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.</p> <p>This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p> <p>Assays for the activation of transcription through the AP1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan</p>
581	HTPBW79	1528	Activation of transcription through AP1 response element in immune cells (such as T-cells).	

581	HTPBW79	1528	Activation of transcription through CD28 response element in immune cells (such as T-cells).	<p>et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is an IL-2 and IL-4 responsive suspension-culture cell line.</p> <p>Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.</p>
581	HTPBW79	1528	Activation of transcription through NFAT response element in immune cells (such as T-cells).	<p>Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Serfling et al., Biochim Biophys Acta 1498(1):1-18 (2000); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-</p>

581	HTPBW79	1528	Activation of transcription through NFKB response element in immune cells (such as T-cells).	<p>844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.</p> <p>Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.</p>
582	HTSEW17	1529	Stimulation of insulin secretion from pancreatic beta cells.	<p>Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and dysregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may</p>

582	HTSEW17	1529	Activation of transcription through NFKB response element in immune cells (such as B-cells).	<p>be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.</p> <p>Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gri G, et al., Biol Chem, 273(11):6431-6438 (1998); Pyatt DW, et al., Cell Biol Toxicol 2000;16(1):41-51 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through the ATCC).</p> <p>Exemplary immune cells that may be used according to these assays include the Reh B-cell line.</p>
583	HTTDB46	1530	Production of IL-4	<p>IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cells, modulate immune cell polarization, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et</p>

583	HTTDB46	1530	<p>al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1994); Yssel et al., Res Immunol 144(8):610-616 (1993); Bagley et al., Nat Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>Assays for the activation of transcription through the NFkB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFkB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFkB response element that may be used or routinely modified to test NFkB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gri G, et al., Biol Chem, 273(11):6431-6438 (1998); Pyatt DW, et al., Cell Biol Toxicol 2000;16(1):41-51 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary immune cells that may be used according to these assays include the Reh B-cell line.</p>
584	HTWCT03	1531	<p>Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of eosinophil cells and cell lines. For example, the CellTiter-Glo Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of</p>

584	HTWCT03	1531	Production of TNF alpha by dendritic cells	<p>metabolically active cells. Eosinophils are a type of immune cell important in allergic responses; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction. Eosinophil cell lines that may be used according to these assays are publicly available and/or may be routinely generated. Exemplary eosinophil cells that may be used according to these assays include EOL-1 Cells.</p> <p>TNFα FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFα), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1998); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.</p>
584	HTWCT03	1531	Production of IL-8 by immune cells (such as the human EOL-1 eosinophil cells)	<p>Assay that measures the production of the chemokine interleukin-8 (IL-8) from immune cells (such as the EOL-1 human eosinophil cell line) are well known in the art (for example, measurement of IL-8 production by FMAT) and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit. Eosinophils are a type of immune cell important in allergic responses; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction. IL-8 is a strong immunomodulator and may have a potential proinflammatory</p>

584	HTWCT03	1531	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	<p>role in immunological diseases and disorders (such as allergy and asthma).</p> <p>This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response development. Exemplary assays for transcription through the GATA3 response element that may be used or routinely modified to test GATA3-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p>
584	HTWCT03	1531	Activation of transcription through NFAT response element in immune cells (such as mast cells).	<p>This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci</p>

584	HTWCT03	1531	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUEVC))	<p>USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p> <p>Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to measure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUEVC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.</p> <p>Endothelial cells, which are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used in ICAM production assays include human umbilical vein endothelial cells (HUEVC), and are available from commercial sources. The expression of ICAM (CD54), a integral membrane protein, can be upregulated by cytokines or other factors, and ICAM expression is important in mediating immune and endothelial cell interactions leading to immune and inflammatory responses. Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays</p>
584	HTWCT03	1531	Production of ICAM in endothelial cells (such as human umbilical vein endothelial cells (HUEVC))	<p>USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p> <p>Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to measure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUEVC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.</p> <p>Endothelial cells, which are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used in ICAM production assays include human umbilical vein endothelial cells (HUEVC), and are available from commercial sources. The expression of ICAM (CD54), a integral membrane protein, can be upregulated by cytokines or other factors, and ICAM expression is important in mediating immune and endothelial cell interactions leading to immune and inflammatory responses. Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays</p>

585	HTWDF76	1532	Activation of transcription through serum response element in immune cells (such as natural killer cells).	<p>disclosed in: Rolfe BE, et al., <i>Atherosclerosis</i>, 149(1):99-110 (2000); Panettieri RA Jr, et al., <i>J Immunol</i>, 154(5):2358-2365 (1995); and, Grunstein MM, et al., <i>Am J Physiol Lung Cell Mol Physiol</i>, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety.</p> <p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., <i>Gene</i> 66:1-10 (1998); Cullen and Malm, <i>Methods in Enzymol</i> 216:362-368 (1992); Henthorn et al., <i>Proc Natl Acad Sci USA</i> 85:6342-6346 (1988); Benson et al., <i>J Immunol</i> 153(9):3862-3873 (1994); and Black et al., <i>Virus Genes</i> 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.</p>
586	HTXAJ12	1533	Activation of Adipocyte ERK Signaling Pathway	<p>Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., <i>Biol Chem</i> 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, <i>Exp Clin Endocrinol Diabetes</i> 107(2):126-132 (1999); Kyriakis JM, <i>Biochem Soc Symp</i> 64:29-48 (1999); Chang and Karin, <i>Nature</i> 410(6824):37-40 (2001); and Cobb MH, <i>Prog Biophys Mol Biol</i> 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that</p>

587	HTXCV12	1534	Activation of transcription through serum response element in immune cells (such as T-cells).	<p>may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p> <p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.</p> <p>Assays for the activation of transcription through the NFkB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFkB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFkB response element that may be used or routinely modified to test NFkB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).</p>
587	HTXCV12	1534	Activation of transcription through NFkB response element in immune cells (such as T-cells).	
588	HTXDW56	1535	Activation of transcription through	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely

588	HTXDW56	1535	<p>NFAT response in immune cells (such as T-cells).</p> <p>modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Serfling et al., Biochim Biophys Acta 1498(1):1-18 (2000); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.</p>
588	HTXDW56	1535	<p>Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Hentinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4 cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).</p>
588	HTXDW56	1535	<p>Assays for the activation of transcription through the NFkB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the</p>

588	HTXDW56	1535	<p>element in immune cells (such as T-cells).</p> <p>Assays for the activation of transcription through the NFkB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFkB transcription factors and modulate expression of neuronal genes. Exemplary assays for transcription through the NFkB response element that may be used or routinely modified to test NFkB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gill JS, et al., <i>Neurobiol Dis</i>, 7(4):448-461 (2000); Tamatani M, et al., <i>J Biol Chem</i>, 274(13):8531-8538 (1999); Berger et al., <i>Gene</i> 66:1-10 (1998); Cullen and Malm, <i>Methods in Enzymol</i> 216:362-368 (1992); Henthorn et al., <i>Proc Natl Acad Sci USA</i> 85:6342-6346 (1988); Black et al., <i>Virus Gnes</i> 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).</p>
588	HTXDW56	1535	<p>Activation of transcription through NFkB response element in neuronal cells (such as SKNMC cells).</p> <p>Assays for the activation of transcription through the NFkB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFkB transcription factors and modulate expression of neuronal genes. Exemplary assays for transcription through the NFkB response element that may be used or routinely modified to test NFkB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gill JS, et al., <i>Neurobiol Dis</i>, 7(4):448-461 (2000); Tamatani M, et al., <i>J Biol Chem</i>, 274(13):8531-8538 (1999); Berger et al., <i>Gene</i> 66:1-10 (1998); Cullen and Malm, <i>Methods in Enzymol</i> 216:362-368 (1992); Henthorn et al., <i>Proc Natl Acad Sci USA</i> 85:6342-6346 (1988); Valle Blazquez et al., <i>Immunology</i> 90(3):455-460 (1997); Aramburau et al., <i>J Exp Med</i> 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Neuronal cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary neuronal cells that may be used according to these assays include the SKNMC neuronal cell line.</p>
588	HTXDW56	1535	<p>Activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or</p>

589	HTXFL30	1536	Activation of transcription through serum response element in immune cells (such as T-cells).	<p>routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Maitikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).</p> <p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.</p> <p>TNFα FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFα), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays</p>
589	HTXFL30	1536	Production of TNF alpha by dendritic cells	<p>TNFα FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFα), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays</p>

589	HTXFL30	1536	Regulation of proliferation and/or differentiation in immune cells (such as mast cells).	<p>disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1998); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.</p> <p>Kinase assays, for example an Elk-1 kinase assay for ERK signal transduction that regulates cell proliferation or differentiation, are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Ali H, et al., J Immunol, 165(12):7215-7223 (2000); Tam SY, et al., Blood, 90(5):1807-1820 (1997); Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Berra et al., Biochem Pharmacol 60(8):1171-1178 (2000); Gupta et al., Exp Cell Res 247(2):495-504 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells that may be used according to these assays include human mast cells such as the HMC-1 cell line.</p>
590	HTXKFP95	1537	Activation of Skeletal Muscle Cell ERK Signalling Pathway	<p>Kinase assay. Kinase assays, for example Elk-1 kinase assays, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes</p>

591	HTXKP61	1538	<p>Activation of transcription through NFKB response element in immune cells (such as T-cells).</p> <p>Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).</p>	<p>107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat myoblast cells that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuses to form multinucleated myotubes and striated fibers after culture in differentiation media.</p>
592	HUDBZ89	1539	<p>Activation of transcription through cAMP response element (CRE) in pre-adipocytes.</p> <p>Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors that activate the cAMP signaling pathway. CREB plays a major role in adipogenesis, and is involved in differentiation into adipocytes. CRE contains the binding sequence for the transcription factor CREB (CRE binding protein). Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al.,</p>	

592	HUDBZ89	1539	Production of GM-CSF	<p>Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Reusch et al., Mol Cell Biol 20(3):1008-1020 (2000); and Klemm et al., J Biol Chem 273:917-923 (1998), the contents of each of which are herein incorporated by reference in its entirety. Pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p> <p>GM-CSF FMat. GM-CSF is expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytes- macrophage progenitors and enhances antimicrobial activity in neutrophils, monocytes and macrophage. Additionally, GM-CSF plays an important role in the differentiation of dendritic cells and monocytes, and increases antigen presentation. GM-CSF is considered to be a proinflammatory cytokine. Assays for immunomodulatory proteins that promote the production of GM-CSF are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and modulate the growth and differentiation of leukocytes. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as GM-CSF, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Ye et al., J Leukoc Biol (58(2):225-233, the contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC) or may be isolated using techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.</p>
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593	HUFBY15	1540	Activation of T-Cell p38 or JNK Signaling Pathway.	<p>Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.</p>
594	HUFEF62	1541	Upregulation of CD152 and activation of T cells	<p>CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oosterveeg et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its</p>

595	HUKAH51	1542	Protection from Endothelial Cell Apoptosis.	<p>entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess the ability of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to inhibit caspase protease-mediated apoptosis. Exemplary assays for caspase apoptosis that may be used or routinely modified to test caspase apoptosis rescue of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Romeo et al., Cardiovasc Res 45(3): 788-794 (2000); Messmer et al., Br J Pharmacol 127(7): 1633-1640 (1999); and J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary endothelial cells that may be used according to these assays include bovine aortic endothelial cells (bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.</p>
595	HUKAH51	1542	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).	<p>Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammatory response</p>

596	HUKBT29	1543	<p>of late stage allergic reaction. Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.</p> <p>Assay to measure regulation of production of Interleukin-6 (IL-6) by either human aortic smooth muscle cells or normal human dermal fibroblasts minus or plus costimulation with TNFalpha (TNFa). Human aortic smooth muscle cells or normal human dermal fibroblasts may be obtained from commercial sources; these cells are important structural and functional components of blood vessels and connective tissue, respectively. Interleukin-6 (IL-6) is a key molecule in chronic inflammation and has been implicated in the progression of atherosclerosis, stroke, arthritis and other vascular and inflammatory diseases. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and production of IL-6.</p>
596	HUKBT29	1543	<p>Production of IL6 by primary human aortic smooth muscle or normal human dermal fibroblast cells (without or with costimulation with TNFalpha).</p> <p>Production of TNF alpha by dendritic cells</p>

596	HUKBT29	1543	Production of IL-4	<p>mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFα), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1998); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.</p> <p>IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cells, modulate immune cell polarization, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1994); Yssel et al., Res Immunol 144(8):610-616 (1993); Bagley et al., Nat Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in</p>
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596	HUKBT29	1543	Production of IL-10 and activation of T-cells.	<p>the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) to modulate IL-10 production and/or T-cell proliferation include, for example, assays such as disclosed and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease" <i>Br Med Bull</i>; 56 (4): 956-968 (2000), and Cohn, et al., "T-helper type 2 cell-directed therapy for asthma" <i>Pharmacology & Therapeutics</i>; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL-10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL-4, IL-10, IL-13, IL-5 and IL-6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.</p>
597	HUSIG64	1544	Activation of transcription through API response element in immune cells (such as T-cells).	<p>Assays for the activation of transcription through the API response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the API response element that may be used or routinely modified to test API-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., <i>Gene</i> 66:1-10 (1988); Cullen and Malm, <i>Methods in Enzymol</i> 216:362-368 (1992); Henthorn et al., <i>Proc Natl Acad Sci USA</i> 85:6342-6346 (1988); Rellahan et al., <i>J Biol Chem</i> 272(49):30806-30811 (1997); Chang et al., <i>Mol Cell Biol</i> 18(9):4986-4993 (1998); and Fraser et al., <i>Eur J Immunol</i> 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Mouse T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary</p>

598	HUSXS50	1545	Activation of T-Cell p38 or JNK Signaling Pathway.	<p>mouse T cells that may be used according to these assays include the HT2 cell line, which is an IL-2 dependent suspension culture cell line that also responds to IL-4.</p> <p>Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., <i>Biol Chem</i> 379(8-9):1101-1110 (1998); Gupta et al., <i>Exp Cell Res</i> 247(2): 495-504 (1999); Kyriakis JM, <i>Biochem Soc Symp</i> 64:29-48 (1999); Chang and Karin, <i>Nature</i> 410(6824):37-40 (2001); and Cobb MH, <i>Prog Biophys Mol Biol</i> 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.</p> <p>Assays for the activation of transcription through the NFkB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFkB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFkB response element that may be used or routinely modified to test NFkB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., <i>Gene</i> 66:1-10 (1998); Cullen and Malm, <i>Methods in Enzymol</i> 216:362-368 (1992); Henthorn et al., <i>Proc Natl Acad Sci USA</i> 85:6342-6346 (1988); Valle Blazquez et al, <i>Immunology</i> 90(3):455-460 (1997); Arambourau et al., <i>J Exp Med</i> 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. For example, a reporter assay (which measures increases in transcription inducible from a NFkB responsive element in EOL-1 cells) may link the NFkB element to a reporter gene and binds to the NFkB transcription factor, which is upregulated by cytokines and other factors. Exemplary immune cells that may be used</p>
598	HUSXS50	1545	Activation of transcription through NFkB response element in immune cells (such as EOL1 cells).	

598	HUSXS50	1545	Calcium flux in immune cells (such as monocytes)	<p>according to these assays include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils are a type of immune cell important in the allergic responses; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction. Eol-1 is a human eosinophil cell line.</p> <p>Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux in immune cells (such as monocytes) include assays disclosed in: Chan, CC, et al., J Pharmacol Exp Ther, 269(3):891-896 (1994); Andersson, K, et al., Cytokine, 12(12):1784-1787 (2000); Scully, SP, et al., J Clin Invest, 74(2) 589-599 (1984); and, Sullivan, E, et al., Methods Mol Biol, 114:125-133 (1999), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the THP-1 monocyte cell line.</p>
599	HVARW53	1546	Activation of transcription through NFAT response element in immune cells (such as mast cells).	<p>This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537</p>

600	HWAAD63	1547	Regulation of transcription through the FAS promoter element in hepatocytes	<p>(1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p> <p>Assays for the regulation of transcription through the FAS promoter element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the FAS promoter element in a reporter construct and to regulate transcription of FAS, a key enzyme for lipogenesis. FAS promoter is regulated by many transcription factors including SREBP. Insulin increases FAS gene transcription in livers of diabetic mice. This stimulation of transcription is also somewhat glucose dependent. Exemplary assays that may be used or routinely modified to test for FAS promoter element activity (in hepatocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Xiong, S., et al., Proc Natl Acad Sci U.S.A., 97(8):3948-53 (2000); Roder, K., et al., Eur J Biochem, 260(3):743-51 (1999); Oskouian B, et al., Biochem J, 317 (Pt 1):257-65 (1996); Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362-368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used according to these assays, such as H4IIE cells, are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays include rat liver hepatoma cell line(s) inducible with glucocorticoids, insulin, or cAMP derivatives.</p>
600	HWAAD63	1547	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	<p>Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to measure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are available from commercial sources. The</p>

600	HWAAD63	1547	Production of ICAM-1	<p>expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.</p> <p>Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).</p>
601	HWABA81	1548	Production of ICAM-1	<p>Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).</p>
601	HWABA81	1548	Upregulation of CD152 and activation of T cells	<p>CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell</p>

602	HWABY10	1549	Production of IL-6	<p>surface markers, such as CD152, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>IL-6 FMTAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when</p>
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602	HWABY10	1549	Activation of transcription through CD28 response element in immune cells (such as T-cells).	<p>activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.</p> <p>Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.</p>
602	HWABY10	1549	Activation of transcription through serum response element in immune cells (such as natural killer cells).	<p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.</p>
603	HWADJ89	1550	Activation of	Assays for the activation of transcription through the Serum Response Element (SRE)

			transcription through serum response element in immune cells (such as T-cells).	are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.
603	HWADJ89	1550	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and dysregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.
604	HWBAO62	1551	Activation of transcription through	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of

605	HWBAR88	1552	CD28 response element in immune cells (such as T-cells).	<p>polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.</p> <p>Assay that measures the production of the chemokine interleukin-8 (IL-8) from immune cells (such as the EOL-1 human eosinophil cell line) are well known in the art (for example, measurement of IL-8 production by FMAT) and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit. Eosinophils are a type of immune cell important in allergic responses; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction. IL8 is a strong immunomodulator and may have a potential proinflammatory role in immunological diseases and disorders (such as allergy and asthma).</p> <p>Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according</p>
605	HWBAR88	1552	Production of IL-8 by immune cells (such as the human EOL-1 eosinophil cells)	<p>Activation of JNK Signaling Pathway in immune cells (such as eosinophils).</p>

606	HWBCB89	1553	<p>to these assays include eosinophils. Eosinophils are important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction. Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.</p> <p>This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response development. Exemplary assays for transcription through the GATA3 response element that may be used or routinely modified to test GATA3-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to</p>

606	HWBCB89	1553	Activation of transcription through NFKB response element in immune cells (such as T-cells).	<p>these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p> <p>Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).</p>
606	HWBCB89	1553	Production of ICAM-1	<p>Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).</p>
606	HWBCB89	1553	Activation of transcription through serum response element in immune cells (such as natural killer cells).	<p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including</p>

607	HWBCP79	1554	Activation of Adipocyte ERK Signaling Pathway	<p>antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.</p> <p>Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p>
607	HWBCP79	1554	Production of IL-10 and activation of T-cells.	<p>Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) to modulate IL-10 production and/or T-cell proliferation include, for example, assays such as disclosed</p>

<p>and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease" Br Med Bull; 56 (4): 956-968 (2000), and Cohn, et al., "T-helper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.</p>				
<p>This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p>	<p>Activation of transcription through NFAT response element in immune cells (such as mast cells).</p>	1555	HWBDP28	608
<p>Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1</p>	<p>Production of ICAM-1</p>	1555	HWBDP28	608

609	HWBFE57	1556	Upregulation of CD71 and activation of T cells	<p>expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).</p> <p>CD71 FMAT. CD71 is the transferrin receptor. Transferrin is a major iron carrying protein that is essential for cell proliferation. CD71 is expressed predominantly on cells that are actively proliferating. Assays for immunomodulatory proteins expressed on activated T cells, B cells, and most proliferating cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD71, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Afetra et al., Ann Rheum Dis 52(6):457-460 (1993), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p>
609	HWBFE57	1556	Upregulation of CD152 and activation of T cells	<p>CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and</p>

610	HWDAC39	1557	Upregulation of CD152 and activation of T cells	<p>agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its</p>
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611	HWDH38	1558	Activation of transcription through serum response element in immune cells (such as T-cells).	<p>entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2): 105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.</p> <p>Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur J Immunol 27(8):1982-1987 (1997); and Masuda et al., J Biol Chem 275(38):29331-29337 (2000), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that</p>
612	HWHGP71	1559	Activation of transcription through STAT6 response element in immune cells (such as T-cells).	

613	HWHGQ49	1560	Activation of transcription through cAMP response element in immune cells (such as T-cells).	<p>may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.</p> <p>Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP and regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.</p>
614	HWHGU54	1561	Activation of transcription through cAMP response element in immune cells (such as T-cells).	<p>Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP and regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.</p>

614	HWHGU54	1561	Production of IL-8 by endothelial cells (such as Human Umbilical Cord Endothelial Cells).	Assays measuring production of IL-8 are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate production and/or secretion of IL-8. For example, FMAT may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate production and/or secretion of IL-8 from endothelial cells (such as human umbilical vein endothelial cells (HUVEC)). HUVECs are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Endothelial cells play a pivotal role in the initiation and perpetuation of inflammation and secretion of IL-8 may play an important role in recruitment and activation of immune cells such as neutrophils, macrophages, and lymphocytes.
615	HWHGZ51	1562	Activation of transcription through GAS response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary mouse T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the CTL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.
615	HWHGZ51	1562	Production of MCP-1	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune

615	HWHGZ51	1562	<p>cell activation. Exemplary assays that test for immunomodulatory proteins evaluate the production of cell surface markers, such as monocyte chemoattractant protein (MCP), and the activation of monocytes and T cells. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.</p> <p>Assays for the activation of transcription through the NFkB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFkB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFkB response element that may be used or routinely modified to test NFkB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. For example, a reporter assay (which measures increases in transcription inducible from a NFkB responsive element in EOL-1 cells) may link the NFkB element to a reporter gene and binds to the NFkB transcription factor, which is upregulated by cytokines and other factors. Exemplary immune cells that may be used according to these assays include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils are a type of immune cell important in the allergic responses; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction. Eol-1 is a human eosinophil cell line.</p>
			<p>Activation of transcription through NFkB response element in immune cells (such as EOL1 cells).</p>

615	HWHGZ51	1562	Upregulation of HLA-DR and activation of T cells	<p>HLA-DR FMAT. MHC class II is essential for correct presentation of antigen to CD4+ T cells. Deregulation of MHC class II has been associated with autoimmune diseases (e.g., diabetes, rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis). Assays for immunomodulatory proteins expressed on MHC class II expressing T cells and antigen presenting cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of MHC class II products, such as HLA-DR antigens, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Lamour et al., Clin Exp Immunol 89(2):217-222 (1992); Hurme and Sihvola, Immunol Lett 20(3):217-222 (1989); Gansbacher and Zier, Cell Immunol 117(1):22-34 (1988); and Itoh et al., J Histochem Cytochem 40(11):1675-1683, the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be</p>
615	HWHGZ51	1562	Upregulation of CD152 and activation of T cells	<p>CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be</p>

616	HWHHL34	1563	<p>used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP and regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.</p>
616	HWHHL34	1563	<p>Activation of transcription through cAMP response element in immune cells (such as T-cells).</p> <p>This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and</p>

				<p>modulate expression of mast cell genes important for immune response development. Exemplary assays for transcription through the GATA3 response element that may be used or routinely modified to test GATA3-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.</p>
617	HWLEV32	1564	Production of IL-4	<p>IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cells, modulate immune cell polarization, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1994); Yssel et al., Res Immunol 144(8):610-616 (1993); Bagley et al., Nat Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and</p>

618	HWLIH65	1565	Activation of T-Cell p38 or JNK Signaling Pathway.	<p>express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.</p> <p>Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.</p>
618	HWLIH65	1565	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	<p>Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMT may be used to measure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.</p>
619	HWTBK81	1566	Proliferation of normal human dermal	<p>Proliferation of smooth muscle cells or fibroblasts is an important component of vascular, fibrotic, and neoplastic diseases. Assays for proliferation of normal human</p>

619	HWTBK81	1566	fibroblast or human primary aortic smooth muscle cells (in the absence or presence of TNFa costimulation).	<p>dermal fibroblasts (NHDF) and human aortic smooth muscle cells (AOSC) (in the absence or presence of TNFa costimulation) are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate NHDF or AOSC cell proliferation. For example, polypeptides of the invention are tested for ability to up-regulate or down-regulate proliferation of NHDF or AOSC cells after culture for four days using Alamar Blue(TM) assay.</p> <p>Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Bruetel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.</p> <p>Assays for the activation of transcription through the NFkB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFkB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFkB response element that may be used or routinely modified to test NFkB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al.,</p>
619	HWTBK81	1566	Activation of Adipocyte ERK Signaling Pathway	<p>Assays for the activation of transcription through the NFkB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFkB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFkB response element that may be used or routinely modified to test NFkB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al.,</p>

620	HYAAJ71	1567	Production of ICAM-1	<p>Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.</p> <p>Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.</p>
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Table 1E

Polynucleotides encoding polypeptides of the present invention can be used in assays to test for one or more biological activities. One such biological activity which may be tested includes the ability of polynucleotides and polypeptides of the invention to stimulate up-regulation or down-regulation of expression of particular genes and proteins. Hence, if polynucleotides and polypeptides of the present invention exhibit activity in altering particular gene and protein expression patterns, it is likely that these polynucleotides and polypeptides of the present invention may be involved in, or capable of effecting changes in, diseases associated with the altered gene and protein expression profiles. Hence, polynucleotides, polypeptides, or antibodies of the present invention could be used to treat said associated diseases.

TaqMan® assays may be performed to assess the ability of polynucleotides (and polypeptides they encode) to alter the expression pattern of particular "target" genes. TaqMan® reactions are performed to evaluate the ability of a test agent to induce or repress expression of specific genes in different cell types. TaqMan® gene expression quantification assays ("TaqMan® assays") are well known to, and routinely performed by, those of ordinary skill in the art. TaqMan® assays are performed in a two step reverse transcription / polymerase chain reaction (RT-PCR). In the first (RT) step, cDNA is reverse transcribed from total RNA samples using random hexamer primers. In the second (PCR) step, PCR products are synthesized from the cDNA using gene specific primers.

To quantify gene expression the Taqman® PCR reaction exploits the 5' nuclease activity of AmpliTaq Gold® DNA Polymerase to cleave a Taqman® probe (distinct from the primers) during PCR. The Taqman® probe contains a reporter dye at the 5'-end of the probe and a quencher dye at the 3' end of the probe. When the probe is intact, the proximity of the reporter dye to the quencher dye results in suppression of the reporter fluorescence. During PCR, if the target of interest is present, the probe specifically anneals between the forward and reverse primer sites. AmpliTaq Fold DNA Polymerase then cleaves the probe between the reporter and quencher when the probe hybridizes to the target, resulting in increased fluorescence of the reporter (see Figure 2). Accumulation of PCR products is detected directly by monitoring the increase in fluorescence of the reporter dye.

After the probe fragments are displaced from the target, polymerization of the strand continues. The 3'-end of the probe is blocked to prevent extension of the probe during PCR. This process occurs in every cycle and does not interfere with the exponential accumulation of product. The increase in fluorescence signal is detected only if the target sequence is complementary to the probe and is amplified during PCR. Because of these requirements, any nonspecific amplification is not detected.

For test sample preparation, vector controls or constructs containing the coding sequence for the gene of interest are transfected into cells, such as for example 293T cells, and supernatants collected after 48 hours. For cell treatment and RNA isolation, multiple primary human cells or human cell lines are used; such cells may include but are not limited to, Normal Human Dermal Fibroblasts, Aortic Smooth Muscle, Human Umbilical Vein Endothelial Cells, HepG2, Daudi, Jurkat, U937, Caco, and THP-1 cell lines. Cells are plated in growth media and growth is arrested by culturing without media change for 3 days, or by switching cells to low serum media and incubating overnight. Cells are treated for 1, 6, or 24 hours with either vector control supernatant or sample supernatant (or purified/partially purified protein preparations in buffer). Total RNA is isolated; for example, by using Trizol extraction or by using the Ambion RNAqueous(TM)-4PCR RNA isolation system. Expression levels of multiple genes are analyzed using TAQMAN, and expression in the test sample is compared to control vector samples to identify genes induced or repressed. Each of the above described techniques are well known to, and routinely performed by, those of ordinary skill in the art.

Table 1E indicates particular disease classes and preferred indications for which polynucleotides, polypeptides, or antibodies of the present invention may be used in detecting, diagnosing, preventing, treating and/or ameliorating said diseases and disorders based on "target" gene expression patterns which may be up- or down-regulated by polynucleotides (and the encoded polypeptides) corresponding to each indicated cDNA Clone ID (shown in Table 1E, Column 2).

Thus, in preferred embodiments, the present invention encompasses a method of detecting, diagnosing, preventing, treating, and/or ameliorating a disease or disorder listed in the "Disease Class" and/or "Preferred Indication" columns of Table 1E; comprising administering to a patient in which such detection, diagnosis, prevention, or treatment is desired a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof) in an amount effective to detect, diagnose, prevent, treat, or ameliorate the disease or disorder. The first and second columns of Table 1D show the "Gene No." and "cDNA Clone ID No.", respectively, indicating certain nucleic acids and proteins (or antibodies against the same) of the invention (including polynucleotide, polypeptide, and antibody fragments or variants thereof) that may be used in detecting, diagnosing, preventing, treating, or ameliorating the disease(s) or disorder(s) indicated in the corresponding row in the "Disease Class" or "Preferred Indication" Columns of Table 1E.

In another embodiment, the present invention also encompasses methods of detecting, diagnosing, preventing, treating, or ameliorating a disease or disorder listed in the "Disease Class" or "Preferred Indication" Columns of Table 1E; comprising administering to a patient combinations of the proteins, nucleic acids, or antibodies of the invention (or fragments or variants thereof), sharing similar indications as shown in the corresponding rows in the "Disease Class" or "Preferred Indication" Columns of Table 1E.

The "Disease Class" Column of Table 1E provides a categorized descriptive heading for diseases, disorders, and/or conditions (more fully described below) that may be detected, diagnosed, prevented, treated, or ameliorated by a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof).

- 5 The "Preferred Indication" Column of Table 1E describes diseases, disorders, and/or conditions that may be detected, diagnosed, prevented, treated, or ameliorated by a protein, nucleic acid, or antibody of the invention (or fragment or variant thereof).

- 10 The "Cell Line" and "Exemplary Targets" Columns of Table 1E indicate particular cell lines and target genes, respectively, which may show altered gene expression patterns (i.e., up- or down-regulation of the indicated target gene) in Taqman assays, performed as described above, utilizing polynucleotides of the cDNA Clone ID shown in the corresponding row. Alteration of expression patterns of the indicated "Exemplary Target" genes is correlated with a particular "Disease Class" and/or "Preferred Indication" as shown in the corresponding row under the respective column headings.

- 15 The "Exemplary Accessions" Column indicates GenBank Accessions (available online through the National Center for Biotechnology Information (NCBI) at <http://www.ncbi.nlm.nih.gov/>) which correspond to the "Exemplary Targets" shown in the adjacent row.

- 20 The recitation of "Cancer" in the "Disease Class" Column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof) may be used for example, to detect, diagnose, prevent, treat, and/or ameliorate neoplastic diseases and/or disorders (e.g., leukemias, cancers, etc., as described below under "Hyperproliferative Disorders").

- 25 The recitation of "Immune" in the "Disease Class" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to detect, diagnose, prevent, treat, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity" "Cardiovascular Disorders" and/or "Blood-Related Disorders"), and infections (e.g., as described below under "Infectious Disease").

- 30 The recitation of "Angiogenesis" in the "Disease Class" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to detect, diagnose, treat, prevent, and/or ameliorate diseases and/or disorders relating to neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), diseases and/or disorders of the cardiovascular system (e.g., as described below under "Cardiovascular Disorders"), diseases and/or disorders involving cellular and genetic abnormalities (e.g., as described below under "Diseases at the Cellular Level"),

diseases and/or disorders involving angiogenesis (e.g., as described below under "Anti-Angiogenesis Activity"), to promote or inhibit cell or tissue regeneration (e.g., as described below under "Regeneration"), or to promote wound healing (e.g., as described below under "Wound Healing and Epithelial Cell Proliferation").

- 5 The recitation of "Diabetes" in the "Disease Class" column indicates that the corresponding nucleic acid and protein, or antibody against the same, of the invention (or fragment or variant thereof), may be used for example, to detect, diagnose, treat, prevent, and/or ameliorate diabetes (including diabetes mellitus types I and II), as well as diseases and/or disorders associated with, or consequential to, diabetes (e.g. as described below under "Endocrine Disorders," "Renal
- 10 Disorders," and "Gastrointestinal Disorders").

Table 1E

Gene No.	cDNA Clone ID	Disease Class	Preferred Indications	Cell Line	Exemplary Targets	Exemplary Accessions
13	HAGDG59	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (AOSMC cells are aortic smooth muscle cells).	AOSMC	Vegf1	gb AF024710 AF024710
13	HAGDG59	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The HEK293 cell line is a human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HEK293	TSP-1	gb X04665 H STHROMR
13	HAGDG59	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (HUVEC cells are human umbilical vein endothelial cells).	HUVEC	Vegf1	gb AF024710 AF024710
13	HAGDG59	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (HUVEC cells are human umbilical vein endothelial cells).	SK-N-MC neuroblastoma	Cycloox Vegf1	gb AF024710 AF024710

13	HAGDG59	Cancer	tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The SK-N-MC neuroblastoma cell line is a cell line derived from human brain tissue available through the ATCC as cell line number HTB-10).	Caco-2	M1 RIBO R p53 TAA6	gb X59543 H SRIREM1 gb X60011 H SP53002 gb J34297 I3 4297
13	HAGDG59	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancer involving cells of the gastrointestinal tract). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving the gastrointestinal tract. (The Caco-2 cell line is a human colorectal adenocarcinoma cell line available through the ATCC as cell line number HTB-37).	HUVEC	bcl-2 Cyclin D	gb X06487 H SBCL2IG gb BC000076 BC000076
13	HAGDG59	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving cells of the brain/ central nervous system (e.g. neural epithelium)). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving the brain or central nervous system. (The SK-N-MC neuroblastoma cell line is a cell line derived from human brain tissue available through the ATCC as cell line number HTB-10).	SK-N-MC neuroblast oma	Bax bcl-2 Cyclin D	gb AF250190 AF250190 gb X06487 H SBCL2IG gb BC000076 BC000076

13	HAGDG59	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes). (The U-937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2)	U937	beta-catenin Cyclin D3 DHFR M1 RIBO R	gb AR03483 2 AR034832 gb V00507 H SDHFR gb X59543 H SRIREM1
13	HAGDG59	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving muscle tissues and the cardiovascular system (e.g. heart, lungs, circulatory system)). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving muscle tissue or the cardiovascular system). (AOSMC cells are human aortic smooth muscle cells).	AOSMC	CIS3 GATA1 IL1B	gb AB00696 7 AB006967 gb X17254 H SERYF1 gb X02532 H SL1BR
13	HAGDG59	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the cells of the gastrointestinal tract). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving cells of the gastrointestinal tract). (The Caco-2 cell line is a human colorectal adenocarcinoma cell line available through the ATCC as cell line number HTB-37).	Caco-2	TNF	gb AJ270944 HSA27094
13	HAGDG59	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving epithelial cells or the renal system). Highly preferred embodiments of the invention include methods of	HEK293	GATA3	gb X55037 H SGATA3

13	HAGDG59	Immune	preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving epithelial cells or the renal system). (The 293 cell line is a human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573). Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving endothelial cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving endothelial cells). (HUVCE cells are human umbilical vein endothelial cells).	HUVEC	CD30 HLA-c IL5 TNF	gb X12705 H SBCDFIA gb AJ270944 HSA27094
13	HAGDG59	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells). (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TIB-152).	Jurkat	Rag1 TNF	gb M29474 H UMRAG1 gb AJ270944 HSA27094
13	HAGDG59	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving cells of the hepatic system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving cells of the hepatic system).	Liver	LTBR	gb AK02708 0 AK027080
13	HAGDG59	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving cells of the hepatic system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving cells of the hepatic system).	SK-N-MC neuroblast oma	CIS3 GATA1 HLA-c	gb AB00696 7 AB006967 gb X17254 H

						SERYFI
13	HAGDG59	Immune	disorders involving the central nervous system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving the central nervous system). (The SK-N-MC neuroblastoma cell line is a cell line derived from human brain tissue and is available through the ATCC as cell line number HTB-10).	T-cell-03/31/00	CD40 Granzyme B	gb AJ300189 HSA30018 gb J04071 H UMCSE
13	HAGDG59	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells).	U937	CD69 TNF	gb Z22576 H SCD69GNA gb AJ270944 HSA27094
79	HCHNF25	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The Caco-2 cell line is a human colorectal adenocarcinoma cell line available through the ATCC as cell line number HTB-37).	Caco-2	ICAM VCAM	gb X06990 H SICAM1 gb A30922 A 30922

79	HCHNF25	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213).	Daudi	Vegf1	gb AF024710 AF024710
79	HCHNF25	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (HUVEC cells are human umbilical vein endothelial cells).	HUVEC	Vegf1	gb AF024710 AF024710
79	HCHNF25	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TB-152).	Jurkat	VCAM	gb A30922 A30922
79	HCHNF25	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TB-152).	NHDF	PAI	gb X12701 H SENDPAI

79	HCHNF25	Angiogenesis	Proliferation. "NHDF cells are normal human dermal fibroblasts). Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The THP-1 cell line is a human monocyte cell line available through the ATCC as cell line number TIB-202).	THP1	Vegf1	gb AF024710 AF024710
79	HCHNF25	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	VCAM	gb A30922 A30922
79	HCHNF25	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of muscle tissues and the cardiovascular system (e.g. heart, lungs, circulatory system)). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders. (AOSMC cells are aortic smooth muscle cells).	AOSMC	Cyclin D2	gb X68452 HSCYCD2
79	HCHNF25	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancer involving cells of the gastrointestinal tract). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving the gastrointestinal tract. (The Caco-2 cell line is a human	Caco-2	c-fos U66469 p53 regulated gene	gb BC004490 BC004490

79	HCHNF25	Cancer	colorectal adenocarcinoma cell line available through the ATCC as cell line number HTB-37). Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as B-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving immune cells (such as B-cells). (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213).	Daudi	Cyclin A1	gb U97680 H SU97680
79	HCHNF25	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving endothelial cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving endothelial cells. (HUVCEC cells are human umbilical vein endothelial cells).	HUVEC	Cyclin A1 Cyclin D Cyclin D2	gb U97680 H SU97680 gb BC000076 BC000076 gb X68452 H SCYCD2
79	HCHNF25	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving immune cells (such as T-cells). (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TIB-152).	Jurkat	DHFR p21 U66469 p53 regulated gene	gb V00507 H SDHFR gb BC000275 BC000275
79	HCHNF25	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving cells of the hepatic system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders	Liver	p21	gb BC000275 BC000275

79	HCHNF25	Cancer	involving cells of the hepatic system. Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes). (The THP-1 cell line is a human monocyte cell line available through the ATCC as cell line number TIB-202).	THP1	c-fos	gb BC004490 BC004490
79	HCHNF25	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes). (The U-937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2)	U937	Cyclin A1 Cyclin D Cyclin D2	gb U97680 H SU97680 gb BC000076 BC000076 gb X68452 H SCYCD2
79	HCHNF25	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the cells of the gastrointestinal tract). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving cells of the gastrointestinal tract). (The Caco-2 cell line is a human colorectal adenocarcinoma cell line available through the ATCC as cell line number HTB-37).	Caco-2	CCR4 CIS3 ICAM VCAM	gb AB02388 8 AB023888 gb AB00696 7 AB006967 gb X06990 H SICAM1 gb A30922 A 30922
79	HCHNF25	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the B-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing,	Daudi	Rag1 Rag2	gb M29474 H UMRAG1 gb AY01196 2 AY011962

79	HCHNF25	Immune	treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving B-cells). (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213).	HUVEC	CD25 TNF	gb X03137 H SIL2RG7 gb AJ270944 HSA27094
79	HCHNF25	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving endothelial cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving endothelial cells). (HUVEC cells are human umbilical vein endothelial cells).	Jurkat	CD28 IL2 VCAM	gb AF222342 AF222342 gb X61155 H SARTIL2 gb A30922 A 30922
79	HCHNF25	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells). (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TIB-152).	Liver	CCR4 CD28 CXCR3 Rag2	gb AB02388 8 AB023888 gb AF222342 AF222342 gb Z79783 H SCKRL2 gb AY01196 2 AY011962
79	HCHNF25	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving cells of the hepatic system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving cells of the hepatic system).	NHDF	CIS3 Rag1	gb AB00696 7 AB006967 gb M29474 H UMRAG1

79	HCHNF25	Immune	invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving the skin). (NHDF cells are normal human dermal fibroblasts). Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The THP1 cell line is a human monocyte cell line available through the ATCC as cell line number TIB-202).	THP1	CD28 CIS3 CXCR3	gb AF222342 AF222342 gb AB00696 7 AB006967 gb Z79783 H SCKRL2
79	HCHNF25	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	TNF VCAM	gb AJ270944 HSA27094 gb A30922 A 30922
105	HDPBQ71	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (AOSMC cells are aortic smooth muscle cells).	AOSMC	FIt1 VCAM	gb AF063657 AF063657 gb A30922 A 30922
105	HDPBQ71	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as	Caco-2	Vegf1	gb AF024710 AF024710

105	HDPBQ71	Angiogenesis	described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The Caco-2 cell line is a human colorectal adenocarcinoma cell line available through the ATCC as cell line number HTB-37). Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213).	Daudi	ICAM	gb X06990 H SICAM1
105	HDPBQ71	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The HEK293 cell line is a human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HEK293	Cycloo x Flt1 iNOS	gb AF063657 AF063657 gb X85761 H SNOS2E3
105	HDPBQ71	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (HUVCEC cells are human umbilical vein endothelial cells).	HUVEC	Flt1 TSP-1 VCAM	gb AF063657 AF063657 gb X04665 H STHROMR gb A30922 A 30922

105	HDPBQ71	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TIB-152).	Jurkat	Flt1 Vegf1	gb AF063657 AF063657 gb AF024710 AF024710
105	HDPBQ71	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation."	Liver	VCAM	gb A30922 A 30922
105	HDPBQ71	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation."	NHDF	TSP-1 Vegf1	gb X04665 H STHROMR gb AF024710 AF024710
105	HDPBQ71	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (NHDF cells are normal human dermal fibroblasts).	T cell	ICAM Vegf1	gb X06990 H SICAM1 gb AF024710 AF024710
105	HDPBQ71	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation."	THP1	VCAM	gb A30922 A

						30922
105	HDPBQ71	Angiogenesis	and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The THP-1 cell line is a human monocyte cell line available through the ATCC as cell line number TIB-202).	U937	VCAM	gb A30922 A 30922
105	HDPBQ71	Cancer	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	Caco-2	p21 TAA6	gb BC000275 BC000275 gb J34297 J3 4297
105	HDPBQ71	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancer involving cells of the gastrointestinal tract). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving the gastrointestinal tract. (The Caco-2 cell line is a human colorectal adenocarcinoma cell line available through the ATCC as cell line number HTB-37).	Daudi	Cyclin D2	gb X68452 H SCYCD2

105	HDPBQ71	Cancer	number CCL-213). Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of epithelial cells or cancers involving the renal system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving epithelial cells or the renal system. (The 293 cell line human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HEK293	c-jun DHFR U66469 p53 regulated gene	gb BC006175 BC006175 gb V00507 H SDHFR
105	HDPBQ71	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving endothelial cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving endothelial cells. (HUVEC cells are human umbilical vein endothelial cells).	HUVEC	beta- catenin Cyclin A1 Cyclin D2	gb U97680 H SU97680 gb X68452 H SCYCD2
105	HDPBQ71	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving cells of the hepatic system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the hepatic system.	Liver	Cyclin D3	gb AR03483 2 AR034832
105	HDPBQ71	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving cells of the skin). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving skin cells. (NHDF cells are normal human dermal fibroblasts).	NHDF	bcl-2 beta- catenin Cyclin D3 DHFR M1 RIBO R U66469 p53	gb X06487 H SBCL2IG gb AR03483 2 AR034832 gb V00507 H SDHFR gb X59543 H SRREM1

105	HDPBQ71	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as T-cells).	T cell	Cyclin D DHFR M1 RIBO R p21	gb BC000076 BC000076 gb V00507 H SDHFR gb X59543 H SRIREM1 gb BC000275 BC000275
105	HDPBQ71	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes). (The THP-1 cell line is a human monocyte cell line available through the ATCC as cell line number TIB-202).	THP1	Cyclin A1 Cyclin D2	gb U97680 H SU97680 gb X68452 H SCYCD2
105	HDPBQ71	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes). (The U-937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2)	U937	Cyclin A1 Cyclin D p21	gb U97680 H SU97680 gb BC000076 BC000076 gb BC000275 BC000275
105	HDPBQ71	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving muscle tissues and the cardiovascular system (e.g. heart, lungs, circulatory system)). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing,	AOSMC	IL1B VCAM	gb X02532 H SIL1BR gb A30922 A 30922

105	HDPBQ71	Immune	treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving muscle tissue or the cardiovascular system). (AOSMC cells are human aortic smooth muscle cells). Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the B-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving B-cells). (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213).	Daudi	c-maf CD25 CXCR3 Granzyme B ICAM	gb AF055377 AF055377 gb X03137 H SIL2RG7 gb Z79783 H SCKRL2 gb J04071 H UMCSE gb X06990 H SICAM1
105	HDPBQ71	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving epithelial cells or the renal system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving epithelial cells or the renal system). (The 293 cell line is a human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HEK293	CCR4 TNF	gb AB02388 8 AB02388 gb AJ270944 HSA27094
105	HDPBQ71	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving endothelial cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving endothelial cells). (HUVVEC cells are human umbilical vein endothelial cells).	HUVVEC	Rag2 VCAM	gb AY01196 2 AY011962 gb A30922 A 30922
105	HDPBQ71	Immune	Highly preferred indications include immunological disorders such as	Jurkat	c-maf	gb AF055377

105	HDPBQ71	Immune	described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells). (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TIB-152).		CD69 TNF	AF055377 gb Z22576 H SCD69GNA gb AJ270944 HSA27094
105	HDPBQ71	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving cells of the hepatic system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving cells of the hepatic system).	Liver	VCAM	gb A30922 A 30922
105	HDPBQ71	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the skin). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving dermal fibroblasts).	NHDF	HLA-c LTBR Rag1	gb AK02708 O AK027080 gb M29474 H UMRAG1
105	HDPBQ71	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the central nervous system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving the central nervous system). (The SK-N-MC neuroblastoma cell line is a cell line derived from human brain tissue and is available through the ATCC as cell line number HTB-10).	SK-N-MC neuroblast oma	CD40 TNF	gb AJ300189 HSA30018 gb AJ270944 HSA27094

105	HDPBQ71	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells).	T cell	CD69 CTLA4 Granzyme B ICAM IFNg IL5 LTBR Rag2	gb Z22576 H SCD69GNA gb AF316875 AF316875 gb J04071 H UMCSE gb X06990 H SICAM1 gb X87308 H SRNAIG gb X12705 H SBCDFIA gb AK02708 Q AK027080 gb AY01196 2 AY011962
105	HDPBQ71	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The THP1 cell line is a human monocyte cell line available through the ATCC as cell line number TIB-202).	THP1	CCR3 CD30 IL6 Rag2 VCAM	gb AB02388 7 AB023887 gb X04403 H S26KDAR gb AY01196 2 AY011962 gb A30922 A 30922
105	HDPBQ71	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	CD69 TNF VCAM	gb Z22576 H SCD69GNA gb AJ270944 HSA27094 gb A30922 A 30922

187	HFCCQ50	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The TF-1 cell line is a human erythroblast cell line available through the ATCC as cell line number CRL-2003).	TF-1	TSP-1	gb X04665 H STHOMR
187	HFCCQ50	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	ICAM	gb X06990 H SICAM1
187	HFCCQ50	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to cancers involving erythrocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving erythrocytes. (The TF-1 cell line is a human erythroblast cell line available through the ATCC as cell line number CRL-2003).	TF-1	Cyclin D2 M1 RIBO R	gb X68452 H SCYCD2 gb X59543 H SRIREM1
187	HFCCQ50	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes). (The U-937 cell line is a human monocyte cell line available through the	U937	Bax DHFR M1 RIBO R	gb AF250190 AF250190 gb V00507 H SDHFR gb X59543 H SRIREM1

187	HFCCQ50	Immune	ATCC as cell line number CRL-1593.2) Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving erythrocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving erythrocytes). (The TF-1 cell line is a human erythroblast cell line available through the ATCC as cell line number CRL-2003).	TF-1	CD40 CD69	gb AJ300189 HSA30018 gb Z22576 H SCD69GNA
187	HFCCQ50	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	ICAM IRF1 LTBR	gb X06990 H SICAM1 gb X14454 H SIRF1 gb AK02708 O AK027080
188	HFCEW05	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to cancers involving erythrocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving erythrocytes. (The TF-1 cell line is a human erythroblast cell line available through the ATCC as cell line number CRL-2003).	TF-1	c-jun p21	gb BC006175 BC006175 gb BC000275 BC000275
188	HFCEW05	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving erythrocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving	TF-1	CD40 IL1B LTBR	gb AJ300189 HSA30018 gb X02532 H SIL1BR gb AK02708 O AK027080

204	HFVAB79	Angiogenesis	erythrocytes). (The TF-1 cell line is a human erythroblast cell line available through the ATCC as cell line number CRL-2003). Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	ICAM	gb X06990 H SICAM1
204	HFVAB79	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes). (The U-937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2)	U937	c-jun	gb BC006175 BC006175
204	HFVAB79	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	CTLA4 ICAM LTBR TNF	gb AF316875 AF316875 gb X06990 H SICAM1 gb AK02708 O AK027080 gb AJ270944 HSA27094
249	HJACG02	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders,"	Adipocyte s-3/12/01	ICAM PAI Vegf1	gb X06990 H SICAM1 gb X12701 H SENDPAI gb AF024710

249	HJACG02	Angiogenesis	"Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (AOSMC cells are aortic smooth muscle cells).	AOSMC	VCAM	gb A30922 A30922	AF024710
249	HJACG02	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213).	Daudi	ICAM VCAM	gb X06990 H SICAM1 gb A30922 A30922	gb X06990 H SICAM1 gb A30922 A30922
249	HJACG02	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (HUVCEC cells are human umbilical vein endothelial cells).	HUVEC	ICAM TSP-1 Vegf1	gb X06990 H SICAM1 gb X04665 H STHROMR gb AF024710 AF024710	gb X06990 H SICAM1 gb X04665 H STHROMR gb AF024710 AF024710
249	HJACG02	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancer involving adipocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or	Adipocyte s-3/12/01	Egr1		

249	HJACG02	Cancer	ameliorating cancer and hyperproliferative disorders. (Primary adipocytes) Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of muscle tissues and the cardiovascular system (e.g. heart, lungs, circulatory system)). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders. (AOSMC cells are aortic smooth muscle cells).	AOSMC	M1 RIBO R	gb X59543 H SRREM1
249	HJACG02	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as B-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving immune cells (such as B-cells). (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213).	Daudi	Cyclin A1	gb U97680 H SU97680
249	HJACG02	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of epithelial cells or cancers involving the renal system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving epithelial cells or the renal system. (The 293 cell line human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HEK293	E- cadherin	gb Z35408 H SECAD9
249	HJACG02	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders	Jurkat	Cyclin A1	gb U97680 H SU97680

249	HJACG02	Cancer	involving immune cells (such as T-cells). (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TIB-152). Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving cells of the hepatic system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the hepatic system.	Liver	Cyclin D2	gb X68452 H SCYCD2
249	HJACG02	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving cells of the skin). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving skin cells. (NHDF cells are normal human dermal fibroblasts).	NHDF	Cyclin A1	gb U97680 H SU97680
249	HJACG02	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving adipocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving adipocytes).	Adipocyte s-3/12/01	ICAM IL6 Rag1	gb X06990 H SICAM1 gb X04403 H S26KDAR gb M29474 H UMRAG1
249	HJACG02	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving muscle tissues and the cardiovascular system (e.g. heart, lungs, circulatory system)). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving muscle tissue or the cardiovascular system). (AOSMC cells are	AOSMC	CD30 CD40 IL1B IL5 TNF VCAM	gb AJ300189 HSA30018 gb X02532 H SIL1BR gb X12705 H SBCDFLA gb AJ270944 HSA27094

			human aortic smooth muscle cells).				gb A30922 A30922
249	HJACG02	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the cells of the gastrointestinal tract). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving cells of the gastrointestinal tract). (The Caco-2 cell line is a human colorectal adenocarcinoma cell line available through the ATCC as cell line number HTB-37).	Caco-2	Rag1	gb M29474 HUMRAG1	
249	HJACG02	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the B-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving B-cells). (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213).	Daudi	ICAM Rag1 VCAM	gb X06990 H SICAM1 gb M29474 H UMRAG1 gb A30922 A30922	
249	HJACG02	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving epithelial cells or the renal system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving epithelial cells or the renal system). (The 293 cell line is a human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HEK293	c-maf	gb AF055377 AF055377	
249	HJACG02	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving epithelial cells or the renal system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving epithelial cells or the renal system). (The 293 cell line is a human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HUVEC	ICAM	gb X06990 H SICAM1	

249	HJACG02	Immune	disorders involving endothelial cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving endothelial cells). (HUVEC cells are human umbilical vein endothelial cells). Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells). (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TIB-152).	Jurkat	Rag2 TNF	gb AY01196 2 AY011962 gb AJ270944 HSA27094
249	HJACG02	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the skin). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving the skin). (NHDF cells are normal human dermal fibroblasts).	NHDF	Rag1	gb M29474 H UMRAG1
249	HJACG02	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	GATA1 IL5 TNF	gb X17254 H SERYF1 gb X12705 H SBCDFLA gb AJ270944 HSA27094
265	HKACD58	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis,	AOSMC	VCAM Vegf1	gb A30922 A 30922

						gb AF024710 AF024710
265	HKACD58	Angiogenesis	wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (AOSMC cells are aortic smooth muscle cells). Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The HEK293 cell line is a human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HEK293	TSP-1 Vegf1	gb X04665 H STHROMR gb AF024710 AF024710
265	HKACD58	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (HUVCEC cells are human umbilical vein endothelial cells).	HUVCEC	ICAM	gb X06990 H SICAM1
265	HKACD58	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (NHDF cells are normal human dermal fibroblasts).	NHDF	VCAM	gb A30922 A 30922
265	HKACD58	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer)	AOSMC	Cyclin D2	gb X68452 H

						SCYCD2
265	HKACD58	Cancer		such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of muscle tissues and the cardiovascular system (e.g. heart, lungs, circulatory system)). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders. (AOSMC cells are aortic smooth muscle cells).	Daudi	c-jun gb BC006175 BC006175
265	HKACD58	Cancer		Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as B-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving immune cells (such as B-cells). (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213).	HEK293	bcl-2 DHFR p21 U66469 p53 regulated gene gb X06487 H SBCL2IG gb V00507 H SDHFR gb BC000275 BC000275
265	HKACD58	Cancer		Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of epithelial cells or cancers involving the renal system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving epithelial cells or the renal system. (The 293 cell line human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HUVEC	U66469 p53 regulated gene
265	HKACD58	Cancer		Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving endothelial cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving endothelial cells. (HUVEC cells are human umbilical vein endothelial cells).	Jurkat	Cyclin D2 gb X68452 H

				such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving immune cells (such as T-cells).(The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TIB-152).				SCYCD2
265	HKACD58	Cancer		Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving cells of the hepatic system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the hepatic system.	Liver	Cyclin D3 Egr1	gb AR03483 2 AR034832	
265	HKACD58	Cancer		Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes).(The THP-1 cell line is a human monocyte cell line available through the ATCC as cell line number TIB-202).	THP1	Cyclin D p21	gb BC0000076 BC0000076 gb BC0000275 BC0000275	
265	HKACD58	Cancer		Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes).(The U-937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	c-jun Cyclin A1	gb BC0006175 BC0006175 gb U97680 H SU97680	
265	HKACD58	Immune		Highly preferred indications include immunological disorders such as	AOSMC	VCAM	gb A30922 A	

					described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving muscle tissues and the cardiovascular system (e.g. heart, lungs, circulatory system)). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving muscle tissue or the cardiovascular system). (AOSMC cells are human aortic smooth muscle cells).			30922
265	HKACD58	Immune		Daudi	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the B-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving B-cells). (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213).	CD40	gb AJ300189 HSA30018	
265	HKACD58	Immune		HUVEC	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving endothelial cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving endothelial cells). (HUVEC cells are human umbilical vein endothelial cells).	ICAM Rag1	gb X06990 H SICAM1 gb M29474 H UMRAG1	
265	HKACD58	Immune		Liver	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving cells of the hepatic system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune	CD28	gb AF222342. AF222342	

265	HKACD58	Immune	disorders involving cells of the hepatic system). Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the skin). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving the skin). (NHDF cells are normal human dermal fibroblasts).	NHDF	CXCR3 GATA1 IL6 VCAM	gb Z79783 H SCKRL2 gb X17254 H SERYF1 gb X04403 H S26KDAR gb A30922 A 30922
265	HKACD58	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The THP1 cell line is a human monocyte cell line available through the ATCC as cell line number TIB-202).	THP1	CIS3	gb AB00696 7 AB006967
265	HKACD58	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	CD69 TNF	gb Z22576 H SCD69GNA gb AJ270944 HSA27094
281	HL2AC08	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving erythrocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving erythrocytes. (The TF-1 cell line is a human erythroblast cell line	TF-1	p21	gb BC000275 BC000275

281	HL2AC08	Immune	available through the ATCC as cell line number CRL-2003). Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving erythrocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving erythrocytes). (The TF-1 cell line is a human erythroblast cell line available through the ATCC as cell line number CRL-2003).	TF-1	CD69 GATA1 TNF	gb Z22576 H SCD69GNA gb X17254 H SER YF1 gb A1270944 HSA27094
389	HNHFO29	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	Flt1 ICAM PAI	gb AF063657 AF063657 gb X06990 H SICAM1 gb X12701 H SENDPAI
389	HNHFO29	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to cancers involving erythrocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving erythrocytes. (The TF-1 cell line is a human erythroblast cell line available through the ATCC as cell line number CRL-2003).	TF-1	bcl-2 Cyclin D DHFR Egr1	gb X06487 H SBCL2IG gb BC000076 BC000076 gb V00507 H SDHFR
389	HNHFO29	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes). (The U-	U937	Cyclin D Cyclin D3 DHFR	gb BC000076 BC000076 gb AR03483 2 AR034832 gb V00507 H SDHFR

389	HNHFO29	Immune	937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2) Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving erythrocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving erythrocytes). (The TF-1 cell line is a human erythroblast cell line available through the ATCC as cell line number CRL-2003).	TF-1	CD40 TNF	gb AJ300189 HSA30018 gb AJ270944 HSA27094
389	HNHFO29	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	ICAM	gb X06990 H SICAM1
495	HSDSB09	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (AOSMC cells are aortic smooth muscle cells).	AOSMC	VCAM	gb A30922 A 30922
495	HSDSB09	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the	Caco-2	ICAM Vegf1	gb X06990 H SICAM1 gb AF024710 AF024710

495	HSDSB09	Angiogenesis	Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The Caco-2 cell line is a human colorectal adenocarcinoma cell line available through the ATCC as cell line number HTB-37). Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The HEK293 cell line is a human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HEK293	Cyclooxygenase VCAM	gb A30922 A30922
495	HSDSB09	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (HUVCE cells are human umbilical vein endothelial cells).	HUVEC	ICAM Vegf1	gb X06990 H SICAM1 gb AF024710 AF024710
495	HSDSB09	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TIB-152).	Jurkat	Flt1	gb AF063657 AF063657
495	HSDSB09	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TIB-152).	Molt4	iNOS	gb X85761 H SNOS2E3

495	HSDSB09	Angiogenesis	wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The Molt4 cell line is a human T cell line available through the ATCC as cell line number CRL-1582).	NHDF	Vegf1	gb AF024710 AF024710
495	HSDSB09	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (NHDF cells are normal human dermal fibroblasts).	SUPT	VCAM	gb A30922 A 30922
495	HSDSB09	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (SUPT cells are human T-cells).	THP1	ICAM TSP-1 VCAM Vegf1	gb X06990 H SICAM1 gb X04665 H STHROMR gb A30922 A 30922 gb AF024710 AF024710
495	HSDSB09	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative	AOSMC	bc1-2 Cyclin A1	gb X06487 H SBCL2IG

			Disorders (particularly including, but not limited to, cancers of muscle tissues and the cardiovascular system (e.g. heart, lungs, circulatory system)). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders. (AOSMC cells are aortic smooth muscle cells).		M1 RIBO R	gb U97680 H SU97680 gb X59543 H SRIREM1
495	HSDSB09	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancer involving cells of the gastrointestinal tract). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving the gastrointestinal tract. (The Caco-2 cell line is a human colorectal adenocarcinoma cell line available through the ATCC as cell line number HTB-37).	Caco-2	DHFR Egr1 p53 U66469 p53 regulated gene	gb V00507 H SDHFR gb X60011 H SP53002
495	HSDSB09	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving immune cells (such as T-cells). (The H9 cell line is a human T lymphocyte cell line available through the ATCC as cell line number HTB-176).	H9	DHFR U66469 p53 regulated gene	gb V00507 H SDHFR
495	HSDSB09	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of epithelial cells or cancers involving the renal system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving epithelial cells or the renal system. (The 293 cell line human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HEK293	bcl-2 Cyclin D E- cadherin M1 RIBO R	gb X06487 H SBCL2IG gb BC000076 BC000076 gb Z35408 H SECAD9 gb X59543 H SRIREM1
495	HSDSB09	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer)	HUVEC	Cyclin D2	gb X68452 H

495	HSDSB09	Cancer	such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving endothelial cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving endothelial cells. (HUVEC cells are human umbilical vein endothelial cells). Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving immune cells (such as T-cells). (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TIB-152).	Jurkat	Cyclin A1 Cyclin D Cyclin D2 Cyclin D3 DHFR Egr1	gb U97680 H SU97680 gb BC000076 BC000076 gb X68452 H SCYCD2 gb AR03483 2 AR034832 gb V00507 H SDHFR	SCYCD2
495	HSDSB09	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving cells of the hepatic system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the hepatic system.	Liver	Cyclin D2 DHFR	gb X68452 H SCYCD2 gb V00507 H SDHFR	SCYCD2
495	HSDSB09	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving immune cells (such as T-cells). (The Molt-4 cell line is a human T-cell line available through the ATCC as cell line number CRL-1582).	Molt4	Cyclin D2 p21	gb X68452 H SCYCD2 gb BC000275 BC000275	SCYCD2

495	HSDSB09	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to cancers involving cells of the skin). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving skin cells. (NHDF cells are normal human dermal fibroblasts).	NHDF	U66469 p53 regulated gene	gb U97680 H SU97680 gb X60011 H SP53002
495	HSDSB09	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to cancers involving cells of the brain/ central nervous system (e.g. neural epithelium)). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving the brain or central nervous system. (The SK-N-MC neuroblastoma cell line is a cell line derived from human brain tissue available through the ATCC as cell line number HTB-10).	SK-N-MC neuroblastoma	Cyclin A1 Egr1 p53 U66469 p53 regulated gene	gb U97680 H SU97680 gb X60011 H SP53002
495	HSDSB09	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes). (The THP-1 cell line is a human monocyte cell line available through the ATCC as cell line number TIB-202).	THP1	Cyclin D DHFR Egr1 p21 U66469 p53 regulated gene	gb BC000076 BC000076 gb V00507 H SDHFR gb BC000275 BC000275
495	HSDSB09	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes). (The U-937 cell line is a human monocyte cell line available through the ATCC as	U937	Egr1	

495	HSDSB09	Immune	cell line number CRL-1593.2) Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving muscle tissues and the cardiovascular system (e.g. heart, lungs, circulatory system)). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving muscle tissue or the cardiovascular system). (AOSMC cells are human aortic smooth muscle cells).	AOSMC	CCR3 CCR4 CD25 CD30 CD40 CTLA4 IL5 Rag1 VCAM	gb AB02388 7 AB023887 gb AB02388 8 AB023888 gb X03137 H SIL2RG7 gb AJ300189 HSA30018 gb AF316875 AF316875 gb X12705 H SBCDFIA gb M29474 H UMRAG1 gb A30922 A 30922
495	HSDSB09	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the cells of the gastrointestinal tract). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving cells of the gastrointestinal tract). (The Caco-2 cell line is a human colorectal adenocarcinoma cell line available through the ATCC as cell line number HTB-37).	Caco-2	c-maf GATA3 ICAM Rag1	gb AF055377 AF055377 gb X55037 H SGATA3 gb X06990 H SICAM1 gb M29474 H UMRAG1
495	HSDSB09	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the B-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system	Daudi	TNF	gb AJ270944 HSA27094

495	HDSB09	Immune	(particularly including, but not limited to, immune disorders involving B-cells). (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213). Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells). (The H9 cell line is a human T lymphocyte cell line available through the ATCC as cell line number HTB-176).	H9	CIS3 Rag1	gb AB00696 7 AB006967 gb M29474 H UMRAG1
495	HDSB09	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving epithelial cells or the renal system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving epithelial cells or the renal system). (The 293 cell line is a human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HEK293	CCR3 CCR4 CD25 CD30 CD40 CTLA4 GATA3 Rag1 TNF VCAM	gb AB02388 7 AB023887 gb AB02388 8 AB023888 gb X03137 H SIL2RG7 gb AJ300189 HSA30018 gb AF316875 AF316875 gb X55037 H SGATA3 gb M29474 H UMRAG1 gb AJ270944 HSA27094 gb A30922 A 30922
495	HDSB09	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving epithelial cells or the renal system). (The 293 cell line is a human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HUVEC	CD40 ICAM IL10	gb AJ300189 HSA30018 gb X06990 H

			disorders involving endothelial cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving endothelial cells). (HUVEC cells are human umbilical vein endothelial cells).		Rag1 Rag2 TNF	SICAM1 gb AF055467 AF055467 gb M29474 H UMRAG1 gb AY01196 2 AY011962 gb AJ270944 HSA27094
495	HSDSB09	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells). (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TIB-152).	Jurkat	CD69 IL5 Rantes TNF	gb Z22576 H SCD69GNA gb X12705 H SBCDFIA gb AF043341 AF043341 gb AJ270944 HSA27094
495	HSDSB09	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving cells of the hepatic system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving cells of the hepatic system).	Liver	CD25	gb X03137 H SIL2RG7
495	HSDSB09	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells). (The Molt-4 cell line is a human T-cell line available through	Molt4	CD28	gb AF222342 AF222342

495	HSDSB09	Immune	the ATCC as cell line number CRL-1582). Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the skin). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving the skin). (NHDF cells are normal human dermal fibroblasts).	NHDF	CD28 CD40 II6	gb AF222342 AF222342 gb AJ300189 HSA30018 gb X04403 H S26KDAR
495	HSDSB09	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the central nervous system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving the central nervous system). (The SK-N-MC neuroblastoma cell line is a cell line derived from human brain tissue and is available through the ATCC as cell line number HTB-10).	SK-N-MC neuroblastoma	c-maf CIS3 TNF	gb AF055377 AF055377 gb AB00696 7 AB006967 gb AJ270944 HSA27094
495	HSDSB09	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells). (The SUPT cell line is a human T-cell line).	SUPT	TNF VCAM	gb AJ270944 HSA27094 gb A30922 A 30922
495	HSDSB09	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes).	THP1	CCR3 CD40 GATA3 ICAM IL5 Rag2 VCAM	gb AB02388 7 AB023887 gb AJ300189 HSA30018 gb X55037 H SGATA3 gb X06990 H

			monocytes). (The THP1 cell line is a human monocyte cell line available through the ATCC as cell line number TIB-202).				SICAM1 gb X12705 H SBCDFIA gb AY01196 2 AY011962 gb A30922 A 30922
495	HSDSB09	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	IL1B		gb X02532 H SL1BR
596	HUKBT29	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to cancers involving erythrocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving erythrocytes. (The TF-1 cell line is a human erythroblast cell line available through the ATCC as cell line number CRL-2003).	TF-1	p21		gb BC000275 BC000275
596	HUKBT29	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes). (The U-937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	p21		gb BC000275 BC000275
596	HUKBT29	Immune	Highly preferred indications include immunological disorders such as	U937	CD69		gb Z22576 H

						SCD69GNA
615	HWHGZ51	Angiogenesis	described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	AOSMC	TSP-1	gb X04665 H STHROMR
615	HWHGZ51	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (AOSMC cells are aortic smooth muscle cells).	Daudi	ICAM PAI	gb X06990 H SICAM1 gb X12701 H SENDPAI
615	HWHGZ51	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213).	H9	VCAM	gb A30922 A 30922
			Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The H9 cell line is a human T lymphocyte cell line available through the ATCC as cell line number HTB-176).			

615	HWHGZ51	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The HEK293 cell line is a human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HEK293	Flt1 iNOS	gb AF063657 AF063657 gb X85761 H SNOS2E3
615	HWHGZ51	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (HUVCEC cells are human umbilical vein endothelial cells).	HUVCEC	Vegf1	gb AF024710 AF024710
615	HWHGZ51	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation."	Liver	Flt1 ICAM PAI VCAM	gb AF063657 AF063657 gb X06990 H SICAM1 gb X12701 H SENDPAI gb A30922 A 30922
615	HWHGZ51	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation."	Molt4	VCAM	gb A30922 A 30922

615	HWHGZ51	Angiogenesis	Proliferation. "(The Molt4 cell line is a human T cell line available through the ATCC as cell line number CRL-1582). Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (NHDF cells are normal human dermal fibroblasts).	NHDF	Vegf1	gb AF024710 AF024710
615	HWHGZ51	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The THP-1 cell line is a human monocyte cell line available through the ATCC as cell line number TIB-202).	THP1	Vegf1	gb AF024710 AF024710
615	HWHGZ51	Angiogenesis	Highly preferred indications include diagnosis, prevention, treatment, and/or amelioration of diseases and disorders involving angiogenesis, wound healing, neoplasia (particularly including, but not limited to, tumor metastases), and cardiovascular diseases and disorders; as described herein under the headings "Hyperproliferative Disorders," "Regeneration," "Anti-Angiogenesis Activity," "Diseases at the Cellular Level," and "Wound Healing and Epithelial Cell Proliferation." (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	ICAM Vegf1	gb X06990 H SICAM1 gb AF024710 AF024710
615	HWHGZ51	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of muscle tissues and the cardiovascular system (e.g. heart, lungs, circulatory system)). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or	AOSMC	Cyclin A1 DHFR	gb U97680 H SU97680 gb V00507 H SDHFR

615	HWHGZ51	Cancer	ameliorating cancer and hyperproliferative disorders. (AOSMC cells are aortic smooth muscle cells). Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancer involving cells of the gastrointestinal tract). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving the gastrointestinal tract. (The Caco-2 cell line is a human colorectal adenocarcinoma cell line available through the ATCC as cell line number HTB-37).	Caco-2	c-fos Cyclin A1	gb BC004490 BC004490 gb U97680 H SU97680
615	HWHGZ51	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as B-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving immune cells (such as B-cells). (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213).	Daudi	Bax	gb AF250190 AF250190
615	HWHGZ51	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of epithelial cells or cancers involving the renal system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving epithelial cells or the renal system. (The 293 cell line human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573).	HEK293	c-jun	gb BC006175 BC006175
615	HWHGZ51	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving endothelial cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or	HUVEC	bcl-2 TAA6	gb X06487 H SBCL2IG gb J34297 J3 4297

615	HWHGZ51	Cancer	ameliorating cancer and hyperproliferative disorders involving endothelial cells.(HUVEC cells are human umbilical vein endothelial cells). Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers involving cells of the hepatic system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the hepatic system.	Liver	Cyclin D3 M1 RBO R U66469 p53 regulated gene	gb AR03483 2 AR034832 gb X59543 H SRIREM1
615	HWHGZ51	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to cancers involving cells of the skin). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving skin cells.(NHDF cells are normal human dermal fibroblasts).	NHDF	bcl-2 TAA6	gb X06487 H SBCL2IG gb J34297 J3 4297
615	HWHGZ51	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes).(The THP-1 cell line is a human monocyte cell line available through the ATCC as cell line number TIB-202).	THP1	DHFR M1 RBO R	gb V00507 H SDHFR gb X59543 H SRIREM1
615	HWHGZ51	Cancer	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancers of immune cells, such as monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving cells of the immune system (such as monocytes).(The U-937 cell line is a human monocyte cell line available through the ATCC as	U937	Cyclin A1	gb U97680 H SU97680

615	HWHGZ51	Diabetes	cell line number CRL-1593.2) A highly preferred indication is diabetes. Additional highly preferred indications include complications associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin). Highly preferred indications also include obesity, weight gain, and weight loss, as well as complications associated with obesity, weight gain, and weight loss. Preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating the above mentioned conditions, disorders, and diseases.	Liver	GAPDH	
615	HWHGZ51	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving muscle tissues and the cardiovascular system (e.g., heart, lungs, circulatory system)). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving muscle tissue or the cardiovascular system). (AOSMC cells are human aortic smooth muscle cells).	AOSMC	CD30 IL6	gb X04403 H S26KDAR

615	HWHGZ51	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the cells of the gastrointestinal tract). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving cells of the gastrointestinal tract). (The Caco-2 cell line is a human colorectal adenocarcinoma cell line available through the ATCC as cell line number HTB-37).	Caco-2	Rag1	gb M29474 H UMRAG1
615	HWHGZ51	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the B-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving B-cells). (The Daudi cell line is a human B lymphoblast cell line available through the ATCC as cell line number CCL-213).	Daudi	CIS3 CXCR3 ICAM	gb AB00696 7 AB006967 gb Z79783 H SCKRL2 gb X06990 H SICAM1
615	HWHGZ51	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells). (The H9 cell line is a human T lymphocyte cell line available through the ATCC as cell line number HTB-176).	H9	IL5 VCAM VLA4	gb X12705 H SBCDFIA gb A30922 A 30922 gb X16983 H SINTAL4
615	HWHGZ51	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving epithelial cells or the renal system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating	HEK293	Rag1 TNF	gb M29474 H UMRAG1 gb AJ270944 HSA27094

615	HWHGZ51	Immune	disorders of the immune system (particularly including, but not limited to, immune disorders involving epithelial cells or the renal system). (The 293 cell line is a human embryonal kidney epithelial cell line available through the ATCC as cell line number CRL-1573). Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving endothelial cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving endothelial cells). (HUV EC cells are human umbilical vein endothelial cells).	HUV EC	CCR7 GATA3 TNF	gb X84702 H SDNABLR2 gb X55037 H SGATA3 gb AJ270944 HSA27094
615	HWHGZ51	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells). (The Jurkat cell line is a human T lymphocyte cell line available through the ATCC as cell line number TIB-152).	Jurkat	Rag1 Rag2	gb M29474 H UMRAG1 gb AY01196 2 A Y011962
615	HWHGZ51	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving cells of the hepatic system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving cells of the hepatic system).	Liver	CCR7 ICAM TNF VCAM	gb X84702 H SDNABLR2 gb X06990 H SICAM1 gb AJ270944 HSA27094 gb A30922 A 30922
615	HWHGZ51	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving cells of the hepatic system).	Molt4	CD25 TNF VCAM	gb X03137 H SIL2RG7 gb AJ270944 HSA27094

			invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells). (The Molt-4 cell line is a human T-cell line available through the ATCC as cell line number CRL-1582).			gb A30922 A30922
615	HWHGZ51	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the skin). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving the skin). (NHDF cells are normal human dermal fibroblasts).	NHDF	CCR7 CD40 GATA3 HLA-c TNF	gb X84702 HSDNABLR2 gb AJ300189 HSA30018 gb X55037 HSGATA3 gb AJ270944 HSA27094
615	HWHGZ51	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving the central nervous system). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving the skin). (The SK-N-MC neuroblastoma and is available through the ATCC as cell line number HTB-10).	SK-N-MC neuroblastoma	CIS3 LTBR Rag1	gb AB006967 AB006967 gb AK027080 AK027080 gb M29474 HUMRAG1
615	HWHGZ51	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells). (The SUPT cell line is a human T-cell line).	SUPT	CCR4 Rag1 TNF	gb AB023888 AB023888 gb M29474 HUMRAG1 gb AJ270944 HSA27094
615	HWHGZ51	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-	THP1	c-maf CCR7	gb AF055377 AF055377

			Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The THP1 cell line is a human monocyte cell line available through the ATCC as cell line number TIB-202).		CXCR3 IL5	gb X84702 H SDNABLR2 gb Z79783 H SCKRL2 gb X12705 H SBCDFIA
615	HWHGZ51	Immune	Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving monocytes). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving monocytes). (The U937 cell line is a human monocyte cell line available through the ATCC as cell line number CRL-1593.2).	U937	CD69 ICAM TNF	gb Z22576 H SCD69GNA gb X06990 H SICAM1 gb AJ270944 HSA27094

Table 2 further characterizes certain encoded polypeptides of the invention, by providing the results of comparisons to protein and protein family databases. The first column provides a unique clone identifier, "Clone ID NO:", corresponding to a cDNA clone disclosed in Table 1A and/or Table 1B. The second column provides the unique contig identifier, "Contig ID:" which allows correlation with the information in Table 1B. The third column provides the sequence identifier, "SEQ ID NO:", for the contig polynucleotide sequences. The fourth column provides the analysis method by which the homology/identity disclosed in the Table was determined. The fifth column provides a description of the PFAM/NR hit identified by each analysis. Column six provides the accession number of the PFAM/NR hit disclosed in the fifth column. Column seven, score/percent identity, provides a quality score or the percent identity, of the hit disclosed in column five. Comparisons were made between polypeptides encoded by polynucleotides of the invention and a non-redundant protein database (herein referred to as "NR"), or a database of protein families (herein referred to as "PFAM"), as described below.

The NR database, which comprises the NBRF PIR database, the NCBI GenPept database, and the SIB SwissProt and TrEMBL databases, was made non-redundant using the computer program nrdb2 (Warren Gish, Washington University in Saint Louis). Each of the polynucleotides shown in Table 1B, column 3 (e.g., SEQ ID NO:X or the 'Query' sequence) was used to search against the NR database. The computer program BLASTX was used to compare a 6-frame translation of the Query sequence to the NR database (for information about the BLASTX algorithm please see Altshul et al., J. Mol. Biol. 215:403-410 (1990), and Gish and States, Nat. Genet. 3:266-272 (1993)). A description of the sequence that is most similar to the Query sequence (the highest scoring 'Subject') is shown in column five of Table 2 and the database accession number for that sequence is provided in column six. The highest scoring 'Subject' is reported in Table 2 if (a) the estimated probability that the match occurred by chance alone is less than 1.0×10^{-7} , and (b) the match was not to a known repetitive element. BLASTX returns alignments of short polypeptide segments of the Query and Subject sequences which share a high degree of similarity; these segments are known as High-Scoring Segment Pairs or HSPs. Table 2 reports the degree of similarity between the Query and the Subject for each HSP as a percent identity in Column 7. The percent identity is determined by dividing the number of exact matches between the two aligned sequences in the HSP, dividing by the number of Query amino acids in the HSP and multiplying by 100. The polynucleotides of SEQ ID NO:X which encode the polypeptide sequence that generates an HSP are delineated by columns 8 and 9 of Table 2.

The PFAM database, PFAM version 2.1, (Sonnhammer, Nucl. Acids Res., 26:320-322, 1998)) consists of a series of multiple sequence alignments; one alignment for each protein family. Each multiple sequence alignment is converted into a probability model called a Hidden Markov

Model, or HMM, that represents the position-specific variation among the sequences that make up the multiple sequence alignment (see, e.g., Durbin, et al., *Biological sequence analysis: probabilistic models of proteins and nucleic acids*, Cambridge University Press, 1998 for the theory of HMMs). The program HMMER version 1.8 (Sean Eddy, Washington University in Saint Louis) was used to compare the predicted protein sequence for each Query sequence (SEQ ID NO:Y in Table 1B.1) to each of the HMMs derived from PFAM version 2.1. A HMM derived from PFAM version 2.1 was said to be a significant match to a polypeptide of the invention if the score returned by HMMER 1.8 was greater than 0.8 times the HMMER 1.8 score obtained with the most distantly related known member of that protein family. The description of the PFAM family which shares a significant match with a polypeptide of the invention is listed in column 5 of Table 2, and the database accession number of the PFAM hit is provided in column 6. Column 7 provides the score returned by HMMER version 1.8 for the alignment. Columns 8 and 9 delineate the polynucleotides of SEQ ID NO:X which encode the polypeptide sequence which show a significant match to a PFAM protein family.

As mentioned, columns 8 and 9 in Table 2, "NT From" and "NT To", delineate the polynucleotides of "SEQ ID NO:X" that encode a polypeptide having a significant match to the PFAM/NR database as disclosed in the fifth column. In one embodiment, the invention provides a protein comprising, or alternatively consisting of, a polypeptide encoded by the polynucleotides of SEQ ID NO:X delineated in columns 8 and 9 of Table 2. Also provided are polynucleotides encoding such proteins, and the complementary strand thereto.

The nucleotide sequence SEQ ID NO:X and the translated SEQ ID NO:Y are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, the nucleotide sequences of SEQ ID NO:X are useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the cDNA contained in ATCC Deposit No:Z. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling immediate applications in chromosome mapping, linkage analysis, tissue identification and/or typing, and a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y may be used to generate antibodies which bind specifically to these polypeptides, or fragments thereof, and/or to the polypeptides encoded by the cDNA clones identified in, for example, Table 1A and/or 1B.

Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA

sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X, and a predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing cDNA ATCC Deposit No:Z (e.g., as set forth in columns 2 and 3 of Table 1A and/or as set forth, for example, in Table 1B, 6, and 7). The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. Further, techniques known in the art can be used to verify the nucleotide sequences of SEQ ID NO:X. The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

Table 2

cDNA Clone ID	Contig ID:	SE Q ID NO :X	Analysis Method	PFam/NR Description	PFam/NR Accession Number	Score/Percent Identity	NT From	NT To
H6EAB28	589947	631	WUblastx.64	(Q9NXY7) CHONDROITIN 4-O-SULFOTRANSFERASE (CHONDROITIN 4-O-SULFOTRANS	Q9NXY7	49% 60% 100% 100% 38% 98%	205 1123 116 1200 1118 413	396 1206 202 1352 1231 1132
HACBD91	637482	16	WUblastx.64	NADH dehydrogenase (ubiquinone) (EC 1.6.5.3) chain NDUFB4 - human	pir JE0383 JE0383	100% 95%	211 1306	357 1368
HACCI17	891114	17	HMMER 2.1.1 WUblastx.64	PFAM: PMP-22/EMP/MP20/Claudin family (AAH19290) Hypothetical 27.7 kDa protein (Fragment)	PF00822 AAH19290	142.7 100%	470 317	1003 1114
HACCI17	731877	632	HMMER 2.1.1 blastx.2	PFAM: PMP-22/EMP/MP20/Claudin family (AF000959) transmembrane protein [Homo sapiens]	PF00822 gb AAC51364.1	35.6 100% 93% 75%	144 311 135 535	329 619 329 786
HADAO89	570689	18	WUblastx.64	(Q9P147) PRO2822.	Q9P147	73%	1106	885
HAGAI85	381942	19	WUblastx.64	(O15432) PROBABLE LOW-AFFINITY COPPER UPTAKE PROTEIN 2 (HCT	COP2_HU MAN	100% 96%	91 228	234 518
HAGAN21	1026956	21	WUblastx.64	(AAH07558) Unknown (protein for MGC:15483).	AAH07558	50% 46%	797 726	708 532
HAGBZ81	456414	22	WUblastx.64	(Q9H291) JUNCTATE.	Q9H291	85% 77%	183 26	329 199
HAGDG59	534165	23	HMMER 2.1.1 WUblastx.64	PFAM: short chain dehydrogenase (Q9UKU4) RETINAL SHORT-CHAIN DEHYDROGENASE/REDUCTASE RETSDR2.	PF00106 Q9UKU4	182.2 96%	232 124	795 1023

HAGFY16	778820	27	WUblastx.64	(Q9BT67) UNKNOWN (PROTEIN FOR MGC:10924).	Q9BT67	100% 72% 100%	183 229 338	221 402 844
HAGFY16	381964	637	blastx.2	(AF220209) Nedd4 WW domain-binding protein 5 [Mus musculus]	gb AAG44248.1	86%	1	720
HAHDB16	635412	28	WUblastx.64	(Q9GMK2) HYPOTHETICAL 10.0 KDA PROTEIN.	Q9GMK2	75% 69%	641 762	522 634
HAHDR32	635357	29	WUblastx.64	(Q9HBU9) POPEYE PROTEIN 2.	Q9HBU9	92%	77	811
HAIBP89	727543	31	WUblastx.64	(Q96G79) Similar to RIKEN cDNA 2610030J16 gene.	Q96G79	99%	290	1261
HAICP19	422672	32	WUblastx.64	(Q9H173) SIL1 PROTEIN PRECURSOR.	Q9H173	100%	83	1465
HAJBR69	638516	35	WUblastx.64	(Q9JIG5) UBIQUITIN SPECIFIC PROTEASE (FRAGMENT).	Q9JIG5	69%	677	48
HAJBZ75	618530	36	WUblastx.64	hypothetical protein DKFZp564D116.1 - human (fragment)	pir T08708 T08708	99%	25	1869
HAMGG68	731859	38	WUblastx.64	(Q9NX85) CDNA FLJ20378 FIS, CLONE KAlA0536.	Q9NX85	71% 44% 57% 70% 56% 64%	984 1454 1457 1458 726 857	859 1401 1416 1429 658 636
HANGG89	852533	639	blastx.2	(AF119297) neuroendocrine-specific protein-like protein 1 [Homo sapiens]	gb AAD26810.1 AF119297_1	99%	59	418
HANGG89	844216	640	WUblastx.64	(AAH08720) Unknown (protein for MGC:8447).	AAH08720	83% 51%	70 490	1017 1068
HANGG89	692291	641	WUblastx.64	(AAH08720) Unknown (protein for MGC:8447).	AAH08720	99% 40%	75 70	1310 198
HAPBS03	656755	40	WUblastx.64	heterogeneous nuclear ribonucleoprotein R - human	pir T02673 T02673	98% 39% 100%	59 68 643	655 136 777
HAPPW30	1352278	43	blastx.14	(AAH20263) Hypothetical 28.7 kDa protein.	AAH20263	91%	59	850

HAPPW30	684272	642	WUblastx.64	(AAH20263) Hypothetical 28.7 kDa protein.	AAH2026 3	100% 36% 100%	54 982 266	263 1056 844
HAPQT22	587601	44	WUblastx.64	(Q9H387) PRO2550.	Q9H387	100%	462 631	439 461
HAPUC89	834358	45	WUblastx.64	(Q9BUM1) UNKNOWN (PROTEIN FOR IMAGE:3050476) (FRAGMENT).	Q9BUM1	99%	109	804
HASAV70	1300782	46	WUblastx.64	(Q9NY08) 19A PROTEIN.	Q9NY08	82%	7	423
HASAV70	381953	643	WUblastx.64	(Q9NY08) 19A PROTEIN.	Q9NY08	100%	4	432
HATAC53	1352276	48	blastx.14	(AAH19903) Hypothetical 29.4 kDa protein (Fragment)	AAH1990 3	100% 100% 39%	64 811 1212	699 840 1280
HATAC53	667830	644	WUblastx.64	(AAH19903) Hypothetical 29.4 kDa protein (Fragment)	AAH1990 3	98% 66%	66 516	593 665
HATBR65	635514	49	WUblastx.64	(Q9H728) CDNA: FLJ21463 FIS, CLONE COL04765.	Q9H728	70% 68%	750 801	610 754
HATCP77	748244	51	WUblastx.64	(Q9Y691) MAXIK CHANNEL BETA 2 SUBUNIT (LARGE CONDUCTANCE CALCIUM-ACTI	Q9Y691	100%	10	582
HBAFJ33	625916	53	WUblastx.64	(Q9GZR7) HYPOTHETICAL 96.3 KDA PROTEIN (ATP-DEPENDENT RNA HELICASE) (Q9GZR7	96%	672	950
HBAFV19	843036	54	WUblastx.64	(Q9H068) HYPOTHETICAL 69.9 KDA PROTEIN.	Q9H068	100%	3	779
HBCPB32	1045580	645	HMMER 2.1.1	PFAM: Sodium Bile acid symporter family	PF01758	41.2	87	-230
			WUblastx.64	(Q96EP9) Unknown (protein for IMAGE:3502817) (Fragment).	Q96EP9	48% 92%	492 2	701 589
HBGNU56	1094642	647	HMMER 2.1.1	PFAM: ATP1G1/PLM/MAT8 family	PF02038	70.5	475	609
			WUblastx.64	(Q96DB9) FXYD domain-containing ion transport regulator 5 p	FXY5_H UMAN	88%	79	612
HBGNU56	1050255	648	HMMER 2.1.1	PFAM: ATP1G1/PLM/MAT8 family	PF02038	70.5	521	655
			WUblastx.64	(Q96DB9) FXYD domain-containing ion transport regulator 5 p	FXY5_H UMAN	88%	125	658
HBHMA23	848016	60	WUblastx.64	(AAH08429) Similar to DNA segment, Chr 2, Massachusetts	AAH0842 9	98% 98%	643 71	1035 649
HBIMB51	963208	61	WUblastx.64	(Q969E3) Urocortin III (Stresscopin).	Q969E3	78%	98	535

HBIMB51	672711	650	WUblastx.64	(Q924A4) Urocortin III.	Q924A4	61%	296	517
HBINS58	1352386	62	blastx.14	(Q9D6W7) 2310047N01RIK PROTEIN.	Q9D6W7	64%	93	302
HBINS58	961712	651	WUblastx.64	(Q9D6W7) 2310047N01RIK PROTEIN.	Q9D6W7	82%	255	578
HBINS58	892924	652	blastx.2	(AF106518) sialomucin CD164 [Homo sapiens]	gb AAC82473.1	64%	177	251
HBIFU48	460392	63	WUblastx.64	(Q9P195) PRO1722.	Q9P195	78%	191	589
HBITY92	778065	64	WUblastx.64	(Q9P529) Hypothetical 15.2 kDa protein.	Q9P529	33%	241	576
HBILCO1	638410	65	WUblastx.64	X-linked retinopathy protein (C-terminal, clone XEH.8c) - human (fragment)	pir A46010 A46010	63%	716	660
HBJLF01	732111	66	HMMER 2.1.1	PFAM: Transmembrane 4 family	PF00335	73%	819	718
HBJNC59	1125802	68	WUblastx.64	(Q9D7W4) 2210021G21RIK PROTEIN.	Q9D7W4	64%	667	533
HBJNC59	899397	653	HMMER 2.1.1	complement subcomponent C1q chain A precursor [validated] - human	pir S14350 C1HUQA	86%	233	2434
HBJNC59	902207	654	blastx.2	(AF135157) complement C1q A chain precursor [Homo sapiens]	gb AAD32626.1 AF135157_1	86%	2325	2432
HBOEG11	1300752	71	WUblastx.64	(O76076) CONNECTIVE TISSUE GROWTH FACTOR-LIKE PROTEIN PRECURSOR (BA44	O76076	86%	2326	2433
HBOEG11	1121709	655	HMMER 2.1.1	PFAM: Insulin-like growth factor binding proteins	PF00219	100%	2348	2434
			WUblastx.64	(O76076) CONNECTIVE TISSUE GROWTH	O76076	96%	2348	2434
						86%	2344	2433
						91%	2333	2434
						65%	829	707
						131.8	223	891
						46%	133	894
						91%	66	800
						30.1	144	245
						79%	77	907
						250.2	409	786
						91%	64	798
						75%	57	806
						45.4	128	340
						75%	53	802

HBOEG11	1049830	656	HMMER 2.1.1 WUblastx.64	FACTOR-LIKE PROTEIN PRECURSOR (BA44 PFAM: Insulin-like growth factor binding proteins (O76076) CONNECTIVE TISSUE GROWTH FACTOR-LIKE PROTEIN PRECURSOR (BA44 (Q9NS11) LIPOPOLYSACCHARIDE SPECIFIC RESPONSE-68 PROTEIN. (AAL36460) POB1.	PF00219 O76076	45.4 100%	122 47	334 796
HBOEG69	793786	72	WUblastx.64		Q9NS11	71% 100%	424 345	314 196
HBXFL29	842802	73	WUblastx.64		AAL3646 0	99%	4	1008
HCACU58	625923	74	WUblastx.64	(Q9NX85) CDNA FLJ20378 FIS, CLONE KALA0536.	Q9NX85	62%	497	820
HCACV51	1306706	75	WUblastx.64	(Q99LM9) UNKNOWN (PROTEIN FOR MGC:8251).	Q99LM9	85%	8	1009
HCACV51	598022	657	WUblastx.64	(Q96BN2) Similar to RIKEN cDNA 2900026B15 gene.	Q96BN2	97% 100%	13 290	312 1015
HCE1Q89	520329	77	WUblastx.64	(Q9NX85) CDNA FLJ20378 FIS, CLONE KALA0536.	Q9NX85	86% 61% 65%	590 645 859	525 592 683
HCE2F54	634016	78	HMMER 2.1.1	PFAM: Histone-like transcription factor (CBF/NF- Y) and archael histone	PF00808	19	868	1005
			WUblastx.64	(AAH07642) Unknown (protein for IMAGE:3534358) (Fra	AAH0764 2	99%	298	1122
HCEFB80	1143407	79	WUblastx.64	(Q96FR3) Unknown (protein for MGC:18083).	Q96FR3	81%	1785	1979
HCEGR33	425212	80	WUblastx.64	(Q9H743) CDNA: FLJ21394 FIS, CLONE COL03536.	Q9H743	51% 42% 58%	1002 1379 907	1079 1492 993
HCEMP62	684780	81	WUblastx.64	(AAL55739) Hypothetical 43.7 kDa protein.	AAL5573 9	94% 94% 40% 94%	484 88 1 870	897 459 198 926
HCEWE17	941941	83	WUblastx.64	(Q9H310) RH TYPE B GLYCOPROTEIN.	Q9H310	84% 92%	9 444	293 566
HCEWE17	893535	660	WUblastx.64	(Q9H310) RH TYPE B GLYCOPROTEIN.	Q9H310	80% 75%	467 695	544 730

HCEWE20	543370	84	WUblastx.64	(Q9P1J1) PRO1546.	Q9P1J1	83%	3	482
HCFOM18	553582	88	WUblastx.64	(Q9H728) CDNA: FLJ21463 FIS, CLONE COL04765.	Q9H728	76% 79%	501 601	551 717
HCHNF25	658672	662	WUblastx.64	(AAH00499) Jumping translocation breakpoint.	AAH00499	60%	621	490
HCMST14	562010	91	WUblastx.64	(Q96DD7) Hypothetical 24.9 kDa protein (Fragment).	Q96DD7	91%	180	620
HCMTB45	862367	92	WUblastx.64	(Q9UI48) PRO0663 (FRAGMENT).	Q9UI48	100%	10	99
HCMTB45	562034	663	WUblastx.64	(Q9UI48) PRO0663 (FRAGMENT).	Q9UI48	67% 61%	748 952	656 914
HCONSM70	637547	95	HMMER 2.1.1 WUblastx.64	PFAM: Immunoglobulin domain (O60487) EPITHELIAL V-LIKE ANTIGEN PRECURSOR (EPITHELIAL V-LIKE ANTIGEN (O60487) EPITHELIAL V-LIKE ANTIGEN PRECURSOR (EPITHELIAL V-LIKE ANTIGEN (O60487) EPITHELIAL V-LIKE ANTIGEN PRECURSOR (EPITHELIAL V-LIKE ANTIGEN (Q60838) SEGMENT POLARITY PROTEIN DISHEVELLED HOMOLOG DVL-2	PF00047 O60487	32% 94%	224 107	481 751
HCONSM70	589445	664	WUblastx.64	similar to Dvl-1 product encoded by GenBank Accession Number 1	O60487	100% 99%	161 408	409 806
HCOOS80	1134974	96	WUblastx.64		DVL2_M OUSE	47% 42% 100%	8 440 636	307 637 677
HCOOS80	1045182	665	blastx.2		gb AAC52827.1	100% 100% 39% 36% 45%	21 588 80 8 444	128 683 163 94 509
HCUCK44	720291	98	WUblastx.64	hypothetical protein DKFZp564J157.1 - human (fragment)	pir T34520 T34520	97%	21	524
HCUEO60	499242	99	WUblastx.64	(Q96MM0) CDNA FLJ32172 fis, clone PLACE6000555.	Q96MM0	79% 72%	1043 1222	972 1028
HCUHK65	651313	100	WUblastx.64	(Q9H3W5) HYPOTHETICAL 79.4 KDA PROTEIN.	Q9H3W5	100%	11	316
HCUHK65	880178	667	HMMER 2.1.1	PFAM: Leucine Rich Repeat	PF00560	92.1	1190	1261

				WUblastx.64	(Q9H3W5) HYPOTHETICAL 79.4 KDA PROTEIN.	Q9H3W5	100%	770	2893
HCWEB58	1352416	102		blastx.14	(Q92WW6) Putative sensor histidine kinase protein.	Q92WW6	36%	355	720
							51%	946	1167
							55%	853	933
							41%	264	335
							37%	757	828
HCWEB58	1115089	668		HMMER 2.1.1	PFAM: Domain found in bacterial signal proteins	PF00672	40.4	442	651
				WUblastx.64	sensor histidine kinase [imported] - Caulobacter crescentus	pirIA8739 6IA87396	36%	379	915
HCWEB58	889268	669		HMMER 2.1.1	PFAM: Domain found in bacterial signal proteins	PF00672	41.6	350	559
				blastx	sensor-like protein [Coxiella burnetii]	gb AAA81939.1	39%	419	829
HCWGU37	1042325	103		WUblastx.64	(Q9H728) CDNA: FLJ21463 FIS, CLONE COL04765.	Q9H728	86%	2588	2523
							77%	2459	2409
							77%	2521	2441
							73%	2373	2329
							70%	2730	2587
HCWKC15	553621	104		WUblastx.64	(Q9NX85) CDNA FLJ20378 FIS, CLONE KAI0536.	Q9NX85	77%	538	419
							56%	710	663
							63%	708	532
HCWUM50	639037	106		WUblastx.64	(Q9NWD1) HYPOTHETICAL 61.6 KDA PROTEIN.	Q9NWD1	92%	1103	1303
							94%	2	175
HCYBG92	598019	107		WUblastx.64	(Q9UPI3) HYPOTHETICAL 57.2 KDA PROTEIN.	Q9UPI3	100%	76	939
HDABR72	1301517	108		WUblastx.64	(Q9BTK4) UNKNOWN (PROTEIN FOR MGC:4663).	Q9BTK4	100%	695	886
HDABR72	748225	671		HMMER 2.1.1	PFAM: Cytochrome P450	PF00067	21.7	145	282
				WUblastx.64	(Q9BTK4) UNKNOWN (PROTEIN FOR MGC:4663).	Q9BTK4	100%	690	881
HDHEB60	499233	109		WUblastx.64	(Q9Y5Y5) PEROXISOMAL BIOGENESIS FACTOR 16.	Q9Y5Y5	81%	277	1284
HDHIA94	765171	110		HMMER 2.1.1	PFAM: Sodium/calcium exchanger protein	PF01699	121.4	178	615
				WUblastx.64	(Q9HC58) SODIUM/CALCIUM EXCHANGER	Q9HC58	98%	10	657

HDHIA94	637576	672	HMMER 2.1.1 blastx.2	NCKX3. PFAM: Sodium/calcium exchanger protein (AF025664) Na-Ca+K exchanger [Bos taurus]	PF01699 gb AAB88 884.1	22.9	187	273
HDHMA72	547772	111	WUblastx.64	(AAH17663) Hypothetical 55.1 kDa protein.	AAH1766 3	28% 95% 50% 99%	3700 761 1019 2	3891 1168 1231 592
HDLAC10	692299	112	WUblastx.64	(Q9UBJ4) TRANSPOSASE-LIKE PROTEIN.	Q9UBJ4	99%	29	1378
HDPBI32	862851	673	WUblastx.64	(O88407) NEURAL MEMBRANE PROTEIN 35.	O88407	95% 89%	599 103	1051 603
HDPBI32	590733	674	HMMER 2.1.1 blastx.2	PFAM: Uncharacterized protein family (AF190461) lifeguard [Homo sapiens]	PF01027 gb AAF06 327.1 AF1 90461_1	126.8 100%	51 15	461 464
HDPBQ71	1160316	115	WUblastx.64	(Q9BRE2) HYPOTHETICAL 68.4 KDA PROTEIN (FRAGMENT).	Q9BRE2	100%	90	1928
HDPBQ71	727200	675	WUblastx.64	(Q9BRE2) HYPOTHETICAL 68.4 KDA PROTEIN (FRAGMENT).	Q9BRE2	99%	21	1859
HDPBQ71	886067	676	WUblastx.64	(Q9H2V9) CDA08.	Q9H2V9	100% 65% 44% 21% 93%	1532 169 182 1456 186	1999 264 322 1551 1541
HDPC191	740748	116	WUblastx.64	(Q9NX17) CDNA FLJ20489 FIS, CLONE KAT08285.	Q9NX17	73% 68% 40%	2372 2545 1570	2548 2685 1674
HDPCY37	837699	118	HMMER 2.1.1 WUblastx.64	PFAM: Glycosyl hydrolase family 47 (Q9H886) CDNA FLJ13869 FIS, CLONE THYRO1001287, WEAKLY SIMILAR TO MAN	PF01532 Q9H886	627.5 92%	199 76	1521 1809
HDPCY37	604114	677	HMMER 2.1.1	PFAM: Glycosyl hydrolase family 47	PF01532	324	199	834
HDPFB02	898208	119	WUblastx.64	(Q9BXR1) COSTIMULATORY MOLECULE.	Q9BXR1	98% 97%	146 877	499 1749

HDPFB02	1056541	678	HMMER 2.1.1 blastx.2	PFAM: Immunoglobulin domain (AF302102) costimulatory molecule [Homo sapiens]	PF00047	97% 76% 53.2 93%	495 568 610 139	620 900 804 1086
HDPFB02	997408	679	HMMER 2.1.1 blastx.2	PFAM: Immunoglobulin domain (AF289028) transmembrane protein B7-H2 ICOS ligand [Homo sapiens]	PF00047	26.9	305	562
HDPFF39	588697	120	WUblastx.64	(O96005) CLEFT LIP AND PALATE TRANSMEMBRANE PROTEIN 1.	gb AAAG01 176.1 AF2 89028_1	90%	266	1123
HDPGP94	823355	123	WUblastx.64	(Q14288) HYPOTHETICAL PROTEIN (FRAGMENT).	Q14288	100% 100% 50% 39% 55% 27% 27% 29%	3 97 689 1093 909 1804 1767 2282	29 762 216 890 700 1652 1090 2082
HDPJF37	704487	125	WUblastx.64	(Q9BSQ8) UNKNOWN (PROTEIN FOR IMAGE:3510191) (FRAGMENT).	Q9BSQ8	94% 36% 93%	105 158 19	650 718 153
HDPMM88	972734	126	HMMER 2.1.1 WUblastx.64	PFAM: E1-E2 ATPase (P98198) POTENTIAL PHOSPHOLIPID- TRANSPORTING ATPASE ID (EC (AF038007) FIC1 [Homo sapiens]	PF00122	31	475	543
HDPMM88	906121	680	blastx.2	(AF038007) FIC1 [Homo sapiens]	AT1D_H UMAN	66% 32%	106 2917	2907 2991
HDPMM88	874074	683	blastx.2	(AF038007) FIC1 [Homo sapiens]	gb AAC63 461.1	62%	3	467
HDPNC61	637585	127	WUblastx.64	(AAG23169) HC6.	gb AAC63 461.1	56%	1023	13
HDPND46	637586	128	WUblastx.64	(Q9BR26) D1257E24.3 (NOVEL PROTEIN) (FRAGMENT).	AAG2316 9	52% 64%	654 37	827 78
HDPOE32	897276	129	WUblastx.64	(Q9BW48) MY047 PROTEIN.	Q9BR26	98%	12	1466
HDPOH06	683371	130	HMMER 2.1.1	PFAM: Uncharacterized membrane protein family	Q9BW48 PF01554	98% 90.8	64 255	345 596

				WUblastx.64	(Q96FL8) Hypothetical 61.9 kDa protein.	Q96FL8	99%	18	977
HDPOZ56	815653	686		HMMER 2.1.1	PFAM: Flavin containing amine oxidase	PF01593	431.1	307	1614
				WUblastx.64	(Q96RQ9) Interleukin-4 induced gene-1 protein.	Q96RQ9	99%	103	1800
HDPOZ56	743479	687		HMMER 2.1.1	PFAM: Flavin containing amine oxidase	PF01593	185.2	200	949
HDPTD15	692917	133		WUblastx.64	(Q9BU29) UNKNOWN (PROTEIN FOR IMAGE:3954899) (FRAGMENT).	Q9BU29	97%	937	833
HDPTK41	744824	134		WUblastx.64	(BAB11849) MOP-2.	BAB11849	97% 99%	1013 72	1126 1025
HDPUG50	684120	135		WUblastx.64	(O60860) GLUCOSYLTRANSFERASE (FRAGMENT).	O60860	99%	4	1599
HDPUH26	866433	136		WUblastx.64	(Q9NXE5) CDNA FLJ20296 FIS, CLONE HEP05890.	Q9NXE5	100%	735	1736
HDPUW68	812737	137		HMMER 2.1.1	PFAM: Immunoglobulin domain	PF00047	38.9	844	1005
				WUblastx.64	(Q9Y286) QA79 MEMBRANE PROTEIN, ALLELIC VARIANT AIRM-1B PRECURSOR.	Q9Y286	95%	70	1440
HDPVW11	1036997	139		HMMER 2.1.1	PFAM: AMP-binding enzyme	PF00501	30.2	913	1344
HDPWN93	992925	140		WUblastx.64	(Q9H747) CDNA: FLJ21347 FIS, CLONE COL02724.	Q9H747	99%	201	2450
HDPWU34	630354	141		HMMER 2.1.1	PFAM: POT family	PF00854	77.2	432	857
				WUblastx.64	(Q9P2X9) PEPTIDE TRANSPORTER 3.	Q9P2X9	100%	3	1091
HDPWU34	701979	692		blastx.2	(AF121080) cAMP inducible 1 protein [Mus musculus]	gb AAD24570.1 AF121080.1	77%	12	242
HDQHD03	1309175	142		WUblastx.64	(O60859) NEUROPATHY TARGET ESTERASE.	O60859	68%	382	1149
HDQHD03	834692	693		HMMER 2.1.1	PFAM: Cyclic nucleotide-binding domain	PF00027	44.3	709	870
				WUblastx.64	(O60859) NEUROPATHY TARGET ESTERASE.	O60859	63%	259	1134
HDTBD53	972757	143		WUblastx.64	(Q9BTV4) UNKNOWN (PROTEIN FOR MGC:3222).	Q9BTV4	100%	183	1382
HDTBP04	1307742	144		WUblastx.64	(Q9DSJ3) 4930432K09RIK PROTEIN.	Q9DSJ3	46%	70	369
HDTBP04	543618	695		WUblastx.64	(Q9DSJ3) 4930432K09RIK PROTEIN.	Q9DSJ3	38%	65	718
HDTDQ23	1306984	145		WUblastx.64	calcium-binding protein (clone pMP41) - mouse (fragment)	pir S04970 S04970	100%	1611	1709

HDTDQ23	879009	696	WUblastx.64	calcium-binding protein (clone pMP41) - mouse (fragment)	pit S04970 S04970	100%	1623	1721
HDTFE17	1043391	148	WUblastx.64	(Q9UJU8) JM24 PROTEIN (FRAGMENT).	Q9UJU8	100% 84% 100%	14 955 343	118 1089 705
HDTFE17	892317	702	HMMER 2.1.1	PFAM: Transmembrane amino acid transporter protein	PF01490	86.4	116	481
HDTIT10	839264	150	HMMER 2.1.1	PFAM: Phosphatidylethanolamine-binding protein (Q96DV4) Similar to RIKEN cDNA 4733401F03 gene.	PF01161	50.9	463	621
			WUblastx.64		Q96DV4	100% 91%	816 352	911 858
HDTIT10	834697	703	blastx.2	(AF117272) O-crystallin [Octopus dofleini] -	gb AAD29640.1 AF117272_1	31%	337	765
HDTMK50	1011485	151	WUblastx.64	(Q9P195) PRO1722.	Q9P195	53% 72% 76%	1119 1186 1331	1030 1121 1176
HE2DY70	722217	152	WUblastx.64	(Q9BS33) SIMILAR TO HYPOTHETICAL PROTEIN FLJ11218.	Q9BS33	100%	9	167
HE2FV03	396139	155	WUblastx.64	(CAD13327) BA382H24.3 (multiple PDZ domain protein)	CAD13327	73%	281	805
HE2NV57	740750	156	WUblastx.64	(Q9UGV6) BK445C9.3 (HIGH-MOBILITY GROUP (NONHISTONE CHROMOSOMAL) PROT	Q9UGV6	31% 66%	321 71	866 106
HE2PD49	638617	157	WUblastx.64	(Q9BSR6) SIMILAR TO RIKEN CDNA 2410018G23 GENE.	Q9BSR6	100%	403	849
HE8DS15	847060	160	WUblastx.64	(Q9WVT0) SEVEN TRANSMEMBRANE RECEPTOR.	Q9WVT0	80% 24% 87%	1 48 269	270 146 985
HE8MH91	589450	161	WUblastx.64	(Q9H8Z4) CDNA FLJ13121 FIS, CLONE NT2RP3002687.	Q9H8Z4	98%	9	410
HE8QV67	1050076	162	WUblastx.64	(BAB55430) CDNA FLJ14978 fis, clone VESEN1000122.	BAB55430	100% 31% 100%	321 487 1	425 600 201

HE9BK23	675382	163	HMMER 2.1.1		PFAM: Fibrinogen beta and gamma chains, C-terminal globular domain (Q9Y5C1) ANGIOPOIETIN 5.	PF00147	84% 74% 86%	1403 577 800	1684 729 1108
HE9DG49	1299935	165	WUblastx.64		(Q9NYL4) FK506 BINDING PROTEIN PRECURSOR.	Q9NYL4	100% 98% 93%	958 39 127	1419 959 618
HE9DG49	658678	707	HMMER 2.1.1		PFAM: FKBP-type peptidyl-prolyl cis-trans isomerases (Q9NYL4) FK506 BINDING PROTEIN PRECURSOR.	PF00254	91	211	492
HE9DG49	382000	708	HMMER 2.1.1		PFAM: FKBP-type peptidyl-prolyl cis-trans isomerases (Q9NYL4) FK506 BINDING PROTEIN PRECURSOR.	Q9NYL4	100%	70	672
HE9OW20	838598	709	WUblastx.64		PFAM: FKBP-type peptidyl-prolyl cis-trans isomerases (CAC41349) Alpha2-glucosyltransferase.	PF00254	91	-71	-352
HE9OW20	834400	710	blastx.2		potassium channel regulator 1 [Rattus norvegicus]	CAC4134	99%	136	1059
HE9RM63	886167	169	WUblastx.64		(Q9NV86) CDNA FLJ10873 FIS, CLONE NT2RP4001730, WEAKLY SIMILAR TO UDP	gb AAC34249.1	81% 90%	449 129	1051 497
HEBCM63	484643	173	WUblastx.64		(Q9BYH1) SEZ6L.	Q9NV86	40% 100%	1995 82	2087 1113
HEBEJ18	701802	174	WUblastx.64		(AAH00573) HSPC163 protein.	Q9BYH1	91%	12	449
HEEAG23	684254	175	HMMER 2.1.1		PFAM: emp24/gp25L/p24 family (Q9CZL0) 2400003B06RIK PROTEIN.	AAH0057	100%	51	467
HEEAJ02	633657	176	WUblastx.64		(Q9BW86) PHOSPHATIDYLETHANOLAMINE N-METHYLTRANSFERASE.	PF01105	36.2	63	185
HEEAQ11	777843	177	HMMER 2.1.1		PFAM: Cystatin domain (Q9H4G1) BA218C14.1 (NOVEL CYSTATIN FAMILY MEMBER).	Q9CZL0	59% 80%	3 406	185 780
HEGAH43	532596	179	WUblastx.64		(Q9HIM5) BA530N10.1 (NOVEL PROTEIN).	Q9BW86	99%	54	761
						PF00031	39.7	360	638
						Q9H4G1	87%	213	653
						Q9HIM5	72%	29	361

HEGAN94	885637	180	WUblastx.64	colipase precursor, pancreatic - dog	pir A4671 7 A46717	36%	148	393
HEGAN94	769649	712	HMMER 2.1.1 WUblastx.64	PFAM: Colipase colipase precursor, pancreatic - dog	PF01114 pir A4671 7 A46717	24 36%	229 229	405 474
HELGK31	681138	182	HMMER 2.1.1 WUblastx.64	PFAM: DHHC zinc finger domain (Q9NPG8) CDNA FLJ10479 FIS, CLONE NT2RP2000120 (DC1) (HYPOTHETICAL 39	PF01529 Q9NPG8	95.1 99%	659 209	820 1240
HELGK31	340352	714	HMMER 2.1.1 blastx.2	PFAM: DHHC zinc finger domain CDNA FLJ10479 FIS, CLONE NT2RP2000120 (DC1).	PF01529 sp Q9NPG 8 Q9NPG 8	95.1 100% 98% 36%	-82 498 242 36	-243 1274 496 128
HELDH85	847372	183	WUblastx.64	(Q9N083) UNNAMED PORTEIN PRODUCT.	Q9N083	52% 53% 67%	1715 1648 1881	1653 1559 1705
HELHL48	696945	184	HMMER 2.1.1 WUblastx.64	PFAM: DHHC zinc finger domain hypothetical protein DKFZp761E1347.1 - human (fragment)	PF01529 pir T4714 4 T47144	124.3 100%	797 359	991 1501
HELHL48	610025	715	HMMER 2.1.1 WUblastx.64	PFAM: DHHC zinc finger domain hypothetical protein DKFZp761E1347.1 - human (fragment)	PF01529 pir T4714 4 T47144	124.3 100% 99% 100%	199 470 585 10	393 586 905 471
HEMAM41	741647	185	WUblastx.64	(AAH21428) Hypothetical 20.0 kDa protein.	AAH2142 8	67%	175	744
HEPAA46	596830	186	WUblastx.64	(Q96PH6) ESC42.	Q96PH6	100%	18	386
HESAJ10	526013	190	WUblastx.64	(AAK95397) Selenoprotein SelM.	AAK9539 7	96% 100% 72%	566 477 550	841 545 582
HETAB45	609827	191	WUblastx.64	(Q9NXH2) CDNA FLJ20254 FIS, CLONE COLF6926.	Q9NXH2	98% 99%	646 3	795 647
HETLM70	1177512	193	WUblastx.64	(Q9H766) CDNA: FLJ21240 FIS, CLONE COL01132.	Q9H766	40%	3	989
HETLM70	1046327	718	blastx.2	B0416.1 gene product [Caenorhabditis elegans]	gb AAB36	30%	231	977

HFABG18	847073	194	WUblastx.64	(Q9QZE9) TM6P1.	841.2 Q9QZE9	95% 88%	53 237	253 797
HFAMB72	490697	195	WUblastx.64	(Q9Y6F6) JAW1-RELATED PROTEIN MR VIIA LONG ISOFORM.	Q9Y6F6	94% 69%	672 1	722 669
HFCCQ50	579993	197	HMMER 2.1.1 WUblastx.64	PFAM: Galactosyltransferase (Q9C0J1) BETA-1,3-N- ACETYLGLUCOSAMINYLTRANSFERASE BGN-T4.	PF01762 Q9C0J1	130.8 95%	365 35	1042 1102
HFAL36	560639	200	WUblastx.64	(O75525) T-STAR.	O75525	100%	568	657
HFAD82	513669	201	WUblastx.64	membrane glycoprotein M6 - mouse	pir I78556 I78556	92%	249	410
HFILZ70	1043350	202	WUblastx.64	(AAK95397) Selenoprotein SelM.	AAK9539 7	100% 92% 96% 91%	990 842 102 423	1145 919 182 458
HFKET18	889515	203	WUblastx.64	(Q9HAD8) CDNA FLJ11786 FIS, CLONE HEMBA1006036.	Q9HAD8	63% 54% 42% 66% 50%	1384 1230 1444 1390 1471	1485 1397 1533 1434 1533
HFKFG02	634743	204	WUblastx.64	ISOFORM OAT1.2 OF O95742	tr_vs O95 742- 01 O9574 2	100% 96%	253 11	564 265
HFPCX09	1309793	208	WUblastx.64	(O95970) LEUCINE-RICH GLIOMA- INACTIVATED PROTEIN PRECURSOR.	O95970	96%	161	1831
HFPCX09	835390	721	HMMER 2.1.1 WUblastx.64	PFAM: Leucine rich repeat C-terminal domain (O95970) LEUCINE-RICH GLIOMA- INACTIVATED PROTEIN PRECURSOR.	PF01463 O95970	46.3 99%	741 225	890 1895
HFPCX09	598723	722	blastx.2	(AF055636) leucine-rich glioma-inactivated protein precursor [Homo sapiens]	gb AAC99 316.1	94% 86%	169 161	1830 298
HFPCX36	526635	209	WUblastx.64	(Q96NR6) CDNA FLJ30278 fis, clone	Q96NR6	56%	680	775

HFTCU19	735139	211	WUblastx.64	BRACE2002755. (Q96B80) Similar to RIKEN cDNA 0610040E02 gene.	Q96B80	66%	450	680
HFTDL56	695976	212	HMMER 2.1.1 WUblastx.64	PFAM: Neurotransmitter-gated ion-channel (P04760) ACETYLCHOLINE RECEPTOR PROTEIN, GAMMA CHAIN PRECUR	PF00065 ACHG_M OUSE	769.9 99%	168 93	1574 1649
HFVAB79	1300736	214	WUblastx.64	(Q9BX93) GROUP XIII SECRETED PHOSPHOLIPASE A2.	Q9BX93	100%	133	693
HFVAB79	565076	724	WUblastx.64	(Q9BX93) GROUP XIII SECRETED PHOSPHOLIPASE A2.	Q9BX93	100%	139	720
HFXTGT26	745381	220	WUblastx.64	(O95662) POT. ORF VI (FRAGMENT).	O95662	57%	162	689
HFXXHK73	609826	223	WUblastx.64	(Q9H960) CDNA FLJ12988 FIS, CLONE NT2RP3000080.	Q9H960	58% 50%	1164 1749	1042 1714
HFXXKJ03	505207	224	WUblastx.64	(O62658) LINE-1 ELEMENT ORF2.	O62658	34% 36%	492 920	292 525
HFXXKT05	658690	225	WUblastx.64	(Q9H5H7) CDNA: FLJ23425 FIS, CLONE HEP22862.	Q9H5H7	81%	5	1015
HFXXKY27	634161	226	WUblastx.64	(Q9H743) CDNA: FLJ21394 FIS, CLONE COL03536.	Q9H743	87% 63% 46%	763 821 936	716 765 814
HGBFO79	422794	227	WUblastx.64	(AAH06833) Similar to DKFZP586F1524 protein.	AAH0683 3	78% 96%	72 134	140 1147
HGBIB74	837220	229	WUblastx.64	hypothetical protein ZK858.6 - Caenorhabditis elegans	pir T2805 8 T28058	50% 51% 65% 62%	1387 2 482 723	1494 439 730 1403
HGBIB74	838602	726	blastx.2	Similar to S.cerevisiae EMP70 protein precursor (S25110) [Homo sapiens]	dbj BAA1 3385.1	87% 100% 78% 88%	736 79 1251 537	1257 477 1505 749
HGBIB74	899864	727	blastx.2	Similar to S.cerevisiae EMP70 protein precursor (S25110) [Homo sapiens]	dbj BAA1 3385.1	87%	12	950
HHAFAF20	838603	231	WUblastx.64	(Q9NXG9) CDNA FLJ20259 FIS, CLONE	Q9NXG9	87%	540	728

HHBCS39	1003028	232	WUblastx.64	COLF7443 (HYPOTHETICAL 47.5 KDA PRO (Q9H763) CDNA: FLJ21269 FIS, CLONE COL01745.	Q9H763	81%	245	580
HHEAA08	638231	233	WUblastx.64	(Q9BVD9) UNKNOWN (PROTEIN FOR MGC:5149).	Q9BVD9	61% 73%	1923 2123	1870 1923
HHEMM74	941955	236	WUblastx.64	(Q96QU0) Calcium-promoted Ras inactivator.	Q96QU0	87%	1741	2046
HHEMM74	906815	731	blastx	unknown [Homo sapiens]	gb AAC50 940.1	61% 53% 71%	830 713 731	738 636 711
HHEPM33	877639	239	WUblastx.64	(Q96BH1) Ring finger protein 25.	Q96BH1	97% 100%	10 1185	1230 1373
HHEPU04	838217	241	WUblastx.64	(Q9BQB6) UNKNOWN (PROTEIN FOR MGC:11276) (PROTEIN FOR IMAGE:3455200).	Q9BQB6	100%	259	747
HHEPU04	897457	734	blastx.2	(BC000828) Unknown (protein for IMAGE:3455200) [Homo sapiens]	gb AAH00 828.1 AA H00828	80%	267	755
HHEPU04	535730	735	WUblastx.64	(Q9BQB6) UNKNOWN (PROTEIN FOR MGC:11276) (PROTEIN FOR IMAGE:3455200).	Q9BQB6	72% 83% 100%	326 217 45	424 339 218
HHFEC49	905849	243	WUblastx.64	(Q9D1N2) 111000219RIK PROTEIN.	Q9D1N2	56%	180	500
HHFFJ48	634521	244	WUblastx.64	(Q9CWA7) 0610010F05RIK PROTEIN (FRAGMENT).	Q9CWA7	88%	1362	1598
HHFGR93	865581	245	WUblastx.64	(Q96AP7) Hypothetical 41.2 kDa protein.	Q96AP7	100%	132	1301
HHFGR93	691402	736	HMMER 2.1.1	PFAM: Immunoglobulin domain	PF00047	36.3	628	807
			WUblastx.64	(Q96AP7) Hypothetical 41.2 kDa protein.	Q96AP7	98% 99%	819 130	1298 828
HHFHR32	411470	247	WUblastx.64	(Q99LX9) SIMILAR TO SINGLE-STRANDED- DNA-BINDING PROTEIN.	Q99LX9	100%	1	762
HHFOJ29	1127491	248	WUblastx.64	(Q9H7P4) FLJ00024 PROTEIN (FRAGMENT).	Q9H7P4	99%	592	65
HHGBO91	520198	249	WUblastx.64	(Q96NR6) CDNA FLJ30278 fis, clone BRACE2002755.	Q96NR6	86% 66% 46% 46%	622 531 439 633	687 620 353 496

HHGCM76	662329	250	WUblastx.64	(Q96FV2) Unknown (protein for IMAGE:3945715) (Fragment).	Q96FV2	94% 98%	7 378	114 536
HHGCM76	383547	739	WUblastx.64	(Q96FV2) Unknown (protein for IMAGE:3945715) (Fragment).	Q96FV2	94% 98%	7 378	114 536
HHGDW43	554613	253	WUblastx.64	(Q9P1J1) PRO1546.	Q9P1J1	59% 52%	707 774	787 887
HHPGO40	1299927	255	WUblastx.64	(Q9HBW1) Brain tumor associated protein NAG14.	Q9HBW1	74% 30%	191 338	976 928
HHPGO40	753270	740	HMMER 2.1.1 WUblastx.64	PFAM: Leucine Rich Repeat (Q9HBW1) Brain tumor associated protein NAG14.	PF00560 Q9HBW1	122% 74% 30%	542 191 338	613 967 928
HHPGO40	560969	741	HMMER 2.1.1	PFAM: Leucine Rich Repeat	PF00560	77%	548	619
HILCF66	636025	258	WUblastx.64	(Q9CWZ1) 240006A19RIK PROTEIN.	Q9CWZ1	100% 96%	1435 1243	1530 1323
HJACG02	1307789	259	WUblastx.64	(Q9HD89) CYSTEINE-RICH SECRETED PROTEIN (C/EBP-EPSILON REGULATED MYEL PROTEIN)	Q9HD89	100%	111	389
HJACG02	509948	742	WUblastx.64	(Q9HD89) CYSTEINE-RICH SECRETED PROTEIN (C/EBP-EPSILON REGULATED MYEL PROTEIN)	Q9HD89	100%	47	370
HJACG30	895505	260	WUblastx.64	(Q9UM21) UDP-GLCNAC-A-1,3-D-MANNOSIDE B-1,4-N-ACETYLGLUCOSAMINYLTRANS	Q9UM21	96%	291	389
HJBCU04	877643	261	WUblastx.64	(Q9Y3P8) SIT PROTEIN PRECURSOR.	Q9Y3P8	100%	36	623
HJBCY35	719729	262	WUblastx.64	hypothetical protein DKFZp586J0619.1 - human (fragment)	pir T0875 8 T08758	100%	1	1212
HJMBM38	545752	264	WUblastx.64	(Q9CS66) 5730496N17RIK PROTEIN (FRAGMENT).	Q9CS66	83%	3	722
HJPAD75	651337	267	WUblastx.64	(Q9H5F8) CDNA: FLJ23476 FIS, CLONE HSI14935.	Q9H5F8	98%	8	232
HKAAB44	564406	269	WUblastx.64	(Q969S6) Unknown (protein for MGC:15961) (protein for MGC:14327).	Q969S6	99%	113	520
HKAAH36	836040	750	WUblastx.64	(AAH08036) Kallikrein 5.	AAH0803 6	90% 100%	184 399	348 1061
HKAAH36	838068	751	HMMER 2.1.1 WUblastx.64	PFAM: Trypsin (AAH08036) Kallikrein 5.	PF00089 AAH0803	270.2% 100%	452 254	1108 1132

HKAAH36	815661	752	HMMER 2.1.1 WUblastx.64	PFAM: Trypsin (AAH08036) Kallikrein 5.	6	270.2	327	983
					AAH0803 6	92%	129	1007
HKAAK02	589945	271	HMMER 2.1.1 WUblastx.64	PFAM: Galactosyltransferase (CAC82374) Beta 1,6-GlcNAc-transferase.	PF01762 4	56.1	457	660
					CAC8237	92%	97	681
HKABZ65	862030	273	WUblastx.64	(Q96LB9) Peptidoglycan recognition protein-I-alpha precursor.	Q96LB9	90%	77	802
						39%	137	541
HKABZ65	665424	754	WUblastx.64	(Q96LB9) Peptidoglycan recognition protein-I-alpha precursor.	Q96LB9	99%	69	794
						45%	129	533
HKACB56	554616	274	HMMER 2.1.1 WUblastx.64	PFAM: Kazal-type serine protease inhibitor domain (P01001) ACROSIN INHIBITORS IIA AND IIB (BUSI-II).	PF00050 IAC2_BO VIN	76.3	114	266
						82%	96	266
HKACD58	552465	755	WUblastx.64	(Q96BH2) Hypothetical 34.4 kDa protein.	Q96BH2	86%	795	1208
						87%	122	724
HKACM93	1352383	277	blastx.14	aqualysin (EC 3.4.21.-) I precursor - Thermus aquaticus	pir A3574 2 A35742	40%	884	1039
						41%	1097	1276
						30%	1274	1468
						50%	746	823
						34%	548	670
						53%	425	469
						58%	2201	2236
HKAEL80	570865	278	WUblastx.64	(Q9H728) CDNA: FLJ21463 FIS, CLONE COL04765.	Q9H728	72%	935	1000
						75%	1002	1073
						61%	763	957
HKAEV06	638238	760	WUblastx.64	(Q9NVA4) CDNA FLJ10846 FIS, CLONE NT2RP4001373.	Q9NVA4	96%	367	459
						100%	197	367
						96%	480	1541
HKAFFK41	545018	280	WUblastx.64	(BAB55101) CDNA FLJ14515 fis, clone NT2RM1000800, w	BAB5510 1	91%	18	371
						60%	130	537
HKAFT66	946512	281	WUblastx.64	(Q9CPS2) 4933428I03RIK PROTEIN.	Q9CPS2	72%	29	61
						62%	82	231

HKAF66	889258	761	blastx	(AF022985) No definition line found [Caenorhabditis elegans]	gb AAB69 975.1	84%	274	828
HKAF66	904790	762	blastx.2	(AJ271091) B-ind1 protein [Homo sapiens]	emb CAB 69070.1	21% 25% 29%	292 562 691	543 702 801
HKDBF34	833065	282	WUblastx.64	(Q9HBJ8) KIDNEY-SPECIFIC MEMBRANE PROTEIN NX-17.	Q9HBJ8	34% 45%	12 298	296 516
HKDBF34	587268	763	WUblastx.64	(Q9HBJ8) KIDNEY-SPECIFIC MEMBRANE PROTEIN NX-17.	Q9HBJ8	88%	69	734
HKGAT94	762811	283	WUblastx.64	(Q9H919) CDNA FLJ13078 FIS, CLONE NT2RP3002002.	Q9H919	73% 80% 63%	307 128 228	239 84 121
HKGAT94	460631	764	blastx.2	pva1 [Plasmodium vivax]	emb CAA 63219.1	41% 62%	456 148	154 116
HKISB57	625956	285	WUblastx.64	(AAL36150) Smoothelin-B3.	AAL3615 0	28% 100% 98% 27% 26% 44%	262 201 1107 271 532 954	582 1013 1256 480 966 1052
HKMLM11	514788	287	WUblastx.64	(Q9P059) HSPC323 (FRAGMENT).	Q9P059	71% 85%	332 148	562 462
HKMLP68	1037919	288	WUblastx.64	(AAH17691) Hypothetical 61.8 kDa protein.	AAH1769 1	42%	8	586
HKMND01	527402	290	WUblastx.64	(Q9H3C0) PRO0898.	Q9H3C0	83%	867	757
HL2AC08	610018	291	HMMER 2.1.1	PFAM: Thioredoxin	PF00085	82.8	145	444
			WUblastx.64	hypothetical protein DKFZp564E1962.1 - human (fragment)	pir T1247 1 T12471	80%	46	903
HLNND09	1172046	293	HMMER 2.1.1	PFAM: PAP2 superfamily	PF01569	20.3	170	352
			WUblastx.64	(Q9H929) CDNA FLJ13055 FIS, CLONE NT2RP3001538, WEAKLY SIMILAR TO HYP PFAM: PAP2 superfamily	Q9H929	88%	107	421
HLNND09	1035153	768	HMMER 2.1.1	PFAM: PAP2 superfamily	PF01569	20.4	62	244

			blastx.2	(AK000307) unnamed protein product [Homo sapiens]	dbj BAA91072.1	50%	2	325
HLD BE54	836041	294	WUblastx.64	(Q9NR71) MITOCHONDRIAL CERAMIDASE.	Q9NR71	98%	212	1051
HLD BE54	600362	769	WUblastx.64	(Q9JHE3) NERUTAL CERAMIDASE (NEUTRAL CERAMIDASE).	Q9JHE3	45%	332	397
						72%	130	306
						78%	375	1028
HLD BE54	800678	770	HMMER 2.1.1	PFAM: Renal dipeptidase	PF01244	466.8	352	1410
			WUblastx.64	(Q9H4A9) PUTATIVE DIPEPTIDASE.	Q9H4A9	95%	133	1590
HLD BX13	815665	295	WUblastx.64	(Q9H387) PRO2550.	Q9H387	76%	1764	1681
						60%	1815	1756
HLD NA86	535730	771	WUblastx.64	(Q9BQB6) UNKNOWN (PROTEIN FOR MGC:11276) (PROTEIN FOR IMAGE:3455200).	Q9BQB6	72%	326	424
						83%	217	339
						100%	45	218
HLD OW79	847396	298	WUblastx.64	(Q90YM5) Organic solute transporter alpha.	Q90YM5	47%	10	672
HLD QC46	847397	299	WUblastx.64	(Q9BXJ8) TRANSMEMBRANE PROTEIN INDUCED BY TUMOR NECROSIS FACTOR ALPHA	Q9BXJ8	100%	28	423
HLD QR62	753742	300	WUblastx.64	(Q9NQW2) PROGRESSIVE ANKYLOSIS-LIKE PROTEIN.	Q9NQW2	100%	41	382
						99%	376	1002
HLD QU79	740755	301	WUblastx.64	(O75477) KE04P.	O75477	100%	105	1142
HLD RM43	846330	302	WUblastx.64	(Q96NZ9) Proline-rich acidic protein.	Q96NZ9	92%	24	476
HLD RM43	638939	772	WUblastx.64	(Q96NZ9) Proline-rich acidic protein.	Q96NZ9	100%	164	616
HLD RP33	647430	303	WUblastx.64	(Q9H743) CDNA: FLJ121394 FIS, CLONE COL03536.	Q9H743	38%	340	278
						64%	599	489
HL HFP03	460467	304	WUblastx.64	(Q9WVC2) LY-6/NEUROTOXIN HOMOLOG (ADULT MALE HIPPOCAMPUS CDNA, RIKEN	Q9WVC2	81%	224	571
HL ICQ90	791828	307	WUblastx.64	(Q96N65) CDNA FLJ1349 fis, clone MESAN2000092, moderately similar to second peroxisomal thioesterase - human	Q96N65	95%	571	636
						93%	59	616
HL QBEO9	520375	309	WUblastx.64		pirJC7367 JC7367	56%	8	559
HL QDR48	1307726	310	WUblastx.64	(Q9NQZ1) HEPATOCELLULAR CARCINOMA ASSOCIATED PROTEIN TD26.	Q9NQZ1	86%	296	406
HL QDR48	619979	776	WUblastx.64	(Q9NQZ1) HEPATOCELLULAR CARCINOMA	Q9NQZ1	83%	289	399

HLTAU74	853614	311	WUblastx.64	ASSOCIATED PROTEIN TD26. (AAH21123) Hypothetical 113.9 kDa protein (Fragment)	AAH2112 3	93% 37%	6 6	704 803
HLTHG37	787530	316	WUblastx.64	(AAH01258) N-acetylglucosamine-phosphate mutase.	AAH0125 8	100% 93%	960 2	1070 955
HLWAA17	629552	317	WUblastx.64	(Q9NY26) IRT1 PROTEIN (SIMILAR TO ZINC/IRON REGULATED TRANSPORTER-LIK	Q9NY26	99%	85	960
HLWAA88	588485	318	WUblastx.64	(Q9H8L6) CDNA FLJ13465 FIS, CLONE PLACE1003493, WEAKLY SIMILAR TO END	Q9H8L6	95% 91% 40% 42% 72%	683 295 781 440 92	1768 696 855 517 322
HLWAA88	769166	778	WUblastx.64	(Q9H8L6) CDNA FLJ13465 FIS, CLONE PLACE1003493, WEAKLY SIMILAR TO END	Q9H8L6	95% 93% 98%	1567 1487 51	1629 1573 1493
HLWAD77	653513	319	WUblastx.64	(Q9GZP9) F-LAN-1 (HYPOTHETICAL TRANSMEMBRANE PROTEIN SBB153).	Q9GZP9	99%	29	745
HLWAE11	783071	320	HMMER 2.1.1 WUblastx.64	PFAM: C1q domain	PF00386 Q9BXI9	44.4 99%	403 28	789 861
HLWAO22	587270	321	WUblastx.64	(Q9BXI9) COMPLEMENT-C1Q TUMOR NECROSIS FACTOR-RELATED PROTEIN. (Q9NRG9) GL003 (ADRAACALIN) (AAAS PROTEIN) (UNKNOWN) (PROTEIN FOR MGC:	Q9NRG9	78% 28% 97% 100% 83% 30% 41% 28% 26% 58%	449 139 1003 14 19 396 503 100 470 333	1147 420 1263 40 495 596 664 408 859 503
HLWAY54	658702	322	WUblastx.64	(Q9BY87) PROACROSIN BINDING PROTEIN SP32 PRECURSOR.	Q9BY87	78% 100% 100%	38 1448 1251	1006 1663 1448

HLWBK05	765310	325	WUblastx.64		(Q9CUS9) 4833416I09RIK PROTEIN (FRAGMENT).	Q9CUS9	23%	1445	1594
HLWBY76	797609	326	WUblastx.64		(AAH06651) Similar to hypothetical protein FLJ23153	AAH06651	37%	1260	1331
HLYAN59	553507	780	WUblastx.64		(Q9P529) Hypothetical 15.2 kDa protein.	Q9P529	80%	1006	1326
							98%	10	1173
							76%	6	1127
							93%	631	720
							96%	638	721
							90%	631	720
							96%	638	721
							96%	638	721
							92%	638	721
							76%	620	721
							89%	638	721
							96%	638	721
							100%	638	721
HL YAZ61	423998	781	HMMER 2.1.1		PFAM: 7 transmembrane receptor (rhodopsin family)	PF00001	71.8	280	-283
			WUblastx.64		(O14626) PROBABLE G PROTEIN-COUPLED RECEPTOR H963.	H963_HUMAN	98%	1	846
HL YES38	638042	334	WUblastx.64		(O95662) POT. ORF VI (FRAGMENT).	O95662	81%	743	856
							72%	281	313
							72%	306	524
							75%	466	735
							33%	145	243
HMADS41	596831	335	WUblastx.64		(AAH07725) Ceroid-lipofuscinosis, neuronal 8 (epile)	AAH07725	92%	186	449
HMADU73	467053	782	WUblastx.64		(Q9EPE8) LOW-DENSITY LIPOPROTEIN RECEPTOR-RELATED PROTEIN 9.	Q9EPE8	100%	427	1041
HMAMI15	1352406	337	blastx.14		(Q96QY4) BA134O15.1 (similar to citrate lyase) (Fragment).	Q96QY4	78%	115	294
							99%	85	1023
HMAMI15	1049263	783	WUblastx.64		(Q96QY4) BA134O15.1 (similar to citrate lyase)	Q96QY4	79%	372	920

HMDAE65	520338	338	WUblastx.64	(Fragment). (Q9NLE3) PROBABLE (HHV-6) U1102, VARIANT A DNA, COMPLETE VIRION GENOM	Q9NLE3	100%	84	440
HMDAM24	514394	339	WUblastx.64	hypothetical protein DKFZp434N0615.1 - human (fragment)	pir T4266 3 T42663	92% 45% 33% 31% 52% 26% 25% 31% 67%	155 298 248 345 877 369 158 318 306	325 363 316 962 984 764 298 818 926
HMECK83	636035	342	WUblastx.64	(O62658) LINE-1 ELEMENT ORF2.	O62658	32% 50% 49%	668 65 483	483 6 100
HMEET96	566720	343	WUblastx.64	(Q9CR48) 2610318G18RIK PROTEIN.	Q9CR48	86%	121	915
HMIAL37	603201	344	HMMER 2.1.1	PFAM: PDZ domain (Also known as DHR or GLGF).	PF00595	57.7	127	327
			WUblastx.64	(Q9Y6N9) ANTIGEN NY-CO-38.	Q9Y6N9	100% 100% 38% 27% 35% 62% 63%	315 76 109 870 765 1111 1067	1100 315 318 1061 998 1242 1132
HMIAP86	726831	345	HMMER 2.1.1	PFAM: Mitochondrial carrier proteins	PF00153	262	329	1180
			WUblastx.64	(AAG29582) Mitochondrial uncoupling protein 5 long	AAG2958 2	97%	182	1183
HMMAH60	562776	347	WUblastx.64	(Q9H728) CDNA: FLJ21463 FIS, CLONE COL04765.	Q9H728	52% 53%	675 820	538 665

HMSBX80	597448	349	WUblastx.64	(Q9H728) CDNA: FLJ21463 FIS, CLONE COL04765.	Q9H728	61%	1721	1413
HMSG14	570833	351	WUblastx.64	(Q9BGV8) HYPOTHETICAL 10.0 KDA PROTEIN.	Q9BGV8	73%	403	615
HMSGT42	383470	352	WUblastx.64	(Q9GZW0) DJ604K5.1 (15 KDA SELENOPROTEIN).	Q9GZW0	91%	40	525
HMSHS36	1127691	354	WUblastx.64	(Q95662) POT. ORF VI (FRAGMENT).	Q95662	83%	781	350
HMSHS36	1028961	785	blastx.2	pot. ORF VI [Homo sapiens]	emb CAA26920.1	61%	539	378
HMSKC04	799540	357	WUblastx.64	(Q9H743) CDNA: FLJ21394 FIS, CLONE COL03536.	Q9H743	77%	609	490
HMTBI36	1301451	358	WUblastx.64	(Q9VZF8) CG1332 PROTEIN.	Q9VZF8	66%	1341	1225
						60%	1414	1346
						56%	1244	1053
						56%	958	2556
						36%	2488	3024
						40%	376	879
						35%	2341	2550
						27%	2494	2622
						40%	712	834
HMTBI36	866466	786	HMMER 2.1.1	PFAM: WD domain, G-beta repeat	PF00400	45.8	2490	2600
			WUblastx.64	(Q9VZF8) CG1332 PROTEIN.	Q9VZF8	56%	948	2555
						37%	2487	3023
						42%	375	878
						35%	2340	2549
						27%	2493	2621
						40%	711	833
						35%	2853	3035
HMUAP70	872208	359	WUblastx.64	(Q9EQH8) NEDD4 WW DOMAIN-BINDING PROTEIN 5 (FRAGMENT).	Q9EQH8	89%	69	845
HMUAP70	778820	788	WUblastx.64	(Q9BT67) UNKNOWN (PROTEIN FOR MGC:10924).	Q9BT67	100%	183	221
						72%	229	402
						100%	338	844
HMUAP70	381964	791	blastx.2	(AF220209) Nedd4 WW domain-binding protein 5 [Mus musculus]	gb AAG44248.1	86%	1	720

HMWEB02	638159	361	WUblastx.64	(Q96MX0) CDNA FLJ1762 fis, clone NT2RI2007754, weakly similar to INT	Q96MX0	100%	10	207
HMWFO02	542061	792	WUblastx.64	(Q9P1C6) PRO2738.	Q9P1C6	61%	647	549
HMWGY65	1308287	363	WUblastx.64	(Q9D624) 1200003C23RIK PROTEIN.	Q9D624	55%	42	1442
HMWGY65	794987	793	WUblastx.64	(AAH19452) Hypothetical 49.0 kDa protein.	AAH1945 2	58%	542	1438
HNEEB45	1036397	365	WUblastx.64	hypothetical protein 3 - human	pir E4192 5 E41925	78%	861	929
HNIFFC43	753337	366	WUblastx.64	(Q96BY8) Hypothetical 55.2 kDa protein.	Q96BY8	39%	523	717
HNFU96	460611	367	WUblastx.64	(Q26195) PVA1 GENE.	Q26195	44%	566	862
HNFJF07	577013	368	WUblastx.64	(AAL55831) Hypothetical 14.1 kDa protein.	AAL5583 1	97%	319	453
HNFJH45	410107	369	WUblastx.64	(Q9H7Z0) CDNA FLJ14058 FIS, CLONE HEMBB1000554.	Q9H7Z0	66%	428	769
HNGAK47	561488	370	WUblastx.64	(Q96EF8) Unknown (protein for MGC:21495).	Q96EF8	54%	177	323
HNGEP09	499076	378	WUblastx.64	(AAK55521) PRO0764.	AAK5552 1	61%	318	371
HNGIJ31	519120	381	WUblastx.64	(Q9N083) UNNAMED PORTEIN PRODUCT.	Q9N083	65%	585	457
						48%	277	11
						33%	12	206
						31%	12	206
						20%	492	617
						34%	492	557
						25%	486	569
						39%	190	2
						29%	537	487
						57%	965	861
						53%	1021	977
						50%	867	715
						73%	566	610

					(Q9HBS7) HYPOTHETICAL 14.2 KDA PROTEIN.			54%	615	725
HNGJE50	561568	383	WUblastx.64			Q9HBS7		66%	454	561
HNGJP69	604891	385	WUblastx.64		(Q9H743) CDNA: FLJ21394 FIS, CLONE COL03536.	Q9H743		53%	973	857
HNGKN89	834857	387	WUblastx.64		(Q9BGZ4) HYPOTHETICAL 11.6 KDA PROTEIN.	Q9BGZ4		71%	860	693
HNGOM56	836064	388	WUblastx.64		(Q96MM0) CDNA FLJ32172 fis, clone PLACE600055.	Q96MM0		67%	891	781
HNHF029	463568	399	WUblastx.64		(Q9NX85) CDNA FLJ20378 FIS, CLONE KAIA0536.	Q9NX85		38%	577	744
HNHOD46	843488	402	WUblastx.64		(O60448) NEURONAL THREAD PROTEIN AD7C-NTP.	O60448		58%	714	953
								69%	522	695
								76%	334	552
								56%	646	921
								56%	645	713
								52%	844	894
								73%	331	498
								59%	353	625
								50%	828	917
								70%	721	792
								48%	781	915
								50%	558	791
								35%	401	595
								31%	283	552
								50%	379	462
								61%	486	839
HNTBI57	570877	405	WUblastx.64		(O95400) CD2 CYTOPLASMIC DOMAIN BINDING PROTEIN (CD2 ANTIGEN (CYTOPLA	O95400		100%	173	1195
HNTCE26	1160395	406	HMMER 2.1.1		PFAM: 7 transmembrane receptor (rhodopsin family)	PF00001		137.5	282	1037
			WUblastx.64		(Q9HIY3) DJ317G22.2 (ENCEPHALOPSIN) (PANOPSIN).	Q9HIY3		100%	111	1316
HNTCE26	853373	801	HMMER 2.1.1		PFAM: 7 transmembrane receptor (rhodopsin family)	PF00001		23.2	63	218

[illegible]

HOACB38	520201	411	WUblastx.64	(Q9H387) PRO2550.	Q9H387	71%	420	295
HODDN65	520348	414	WUblastx.64	(Q9N083) UNNAMED PORTEIN PRODUCT.	Q9N083	77%	589	419
HODDN92	422913	415	WUblastx.64	(Q9H1S5) BA110H4.2 (SIMILAR TO MEMBRANE PROTEIN).	Q9H1S5	74%	743	663
HODDO08	790333	416	WUblastx.64	(AAL55740) Hypothetical 11.9 kDa protein.	AAL55740	67%	660	493
HODDW40	579256	417	WUblastx.64	(Q9NX85) CDNA FLJ20378 FIS, CLONE KAIA0536.	Q9NX85	100%	1119	1021
HODGE68	834907	420	WUblastx.64	retrovirus-related hypothetical protein II - human 1	pir S23650	100%	725	1042
HOEBK34	768325	421	HMMER 2.1.1	PFAM: von Willebrand factor type C domain	S23650	36%	370	278
			WUblastx.64	(O94769) EXTRACELLULAR MATRIX PROTEIN.	PF00093	54%	276	1
HOEBK34	509951	806	WUblastx.64	(O94769) EXTRACELLULAR MATRIX PROTEIN.	O94769	54.1	455	619
HOEBZ89	828177	422	WUblastx.64	hypothetical protein C05G5.5 - Caenorhabditis elegans	pir T18967	96%	149	643
HOEDB32	634994	423	WUblastx.64	(Q9Y2Y6) TADA1 PROTEIN (DKFZP564K1964 PROTEIN).	Q9Y2Y6	93%	133	1008
HOEDE28	1036480	424	WUblastx.64	(AAG23764) PP3686.	AAG23764	31%	104	781
HOEDH84	748236	425	WUblastx.64	(Q960D8) SD05564p.	AAG23764	95%	933	1535
HOEFV61	833079	426	HMMER 2.1.1	PFAM: Leucine Rich Repeat	4	99%	7	1449
			WUblastx.64	(Q9C000) NAC-BETA SPLICE VARIANT.	Q960D8	39%	142	216
					PF00560	22	695	1507
					Q9C000	97%	1496	1969
						94%	1163	1300
						36%	10	555
						100%	1419	1460
						57%	303	434
						29%	1945	2001
						100%	127	489

HOFC33	1184465	427	WUblastx.64	(O15232) MATRILIN-3 PRECURSOR.		34%	555	659
HOFC33	919896	808	HMMER 2.1.1 WUblastx.64	PFAM: von Willebrand factor type A domain (O15232) MATRILIN-3 PRECURSOR.	MTN3_H UMAN	189.8	288	815
HOFC33	906694	809	HMMER 2.1.1	PFAM: von Willebrand factor type A domain	PF00092	85%	204	1499
HOFC33	911180	428	HMMER 2.1.1 WUblastx.64	PFAM: Eukaryotic aspartyl protease cathepsin D (EC 3.4.23.5) precursor [validated] - human	MTN3_H UMAN	162.2	318	737
HOFC33	892291	814	HMMER 2.1.1 WUblastx.64	PFAM: Eukaryotic aspartyl protease cathepsin D (EC 3.4.23.5) precursor [validated] - human	PF00092	619	290	1303
HOFC33	847424	430	HMMER 2.1.1 WUblastx.64	PFAM: Cadherin domain (AAK51617) Protocadherin-beta7.	pirA2577 1[KHHUD	81%	83	1303
HOFC33	1186156	432	WUblastx.64	clusterin precursor - dog	PF00026	496.2	336	1232
HOFC33	967554	816	HMMER 2.1.1 WUblastx.64	PFAM: Clusterin clusterin precursor - dog	pirA2577 1[KHHUD	96%	192	1232
HOFC33	878690	817	HMMER 2.1.1	PFAM: Clusterin	PF00028	256	905	1180
HOFC33	905734	818	HMMER 2.1.1 blastx.2	glycoprotein 80 [Canis familiaris]	AAK5161 7	83%	167	2047
HOFC33	806819	821	HMMER 2.1.1 WUblastx.64	PFAM: 60s Acidic ribosomal protein acidic ribosomal protein P0, cytosolic [validated] - human	pirA4001 8/A40018	30%	425	1858
HOFC33	806819	821	HMMER 2.1.1 WUblastx.64	PFAM: 60s Acidic ribosomal protein acidic ribosomal protein P0, cytosolic [validated] - human	pirA4001 8/A40018	69%	1022	1414
HOFC33	806819	821	HMMER 2.1.1 WUblastx.64	PFAM: 60s Acidic ribosomal protein acidic ribosomal protein P0, cytosolic [validated] - human	pirA4001 8/A40018	81%	115	1086
HOFC33	806819	821	HMMER 2.1.1 WUblastx.64	PFAM: 60s Acidic ribosomal protein acidic ribosomal protein P0, cytosolic [validated] - human	PF01093	236.4	81	395
HOFC33	806819	821	HMMER 2.1.1 WUblastx.64	PFAM: 60s Acidic ribosomal protein acidic ribosomal protein P0, cytosolic [validated] - human	pirA4001 8/A40018	65%	120	449
HOFC33	806819	821	HMMER 2.1.1 WUblastx.64	PFAM: 60s Acidic ribosomal protein acidic ribosomal protein P0, cytosolic [validated] - human	PF01093	236.6	81	395
HOFC33	806819	821	HMMER 2.1.1 WUblastx.64	PFAM: 60s Acidic ribosomal protein acidic ribosomal protein P0, cytosolic [validated] - human	PF01093	301.2	76	432
HOFC33	806819	821	HMMER 2.1.1 WUblastx.64	PFAM: 60s Acidic ribosomal protein acidic ribosomal protein P0, cytosolic [validated] - human	gblAAA30 846.1	81%	440	1087
HOFC33	806819	821	HMMER 2.1.1 WUblastx.64	PFAM: 60s Acidic ribosomal protein acidic ribosomal protein P0, cytosolic [validated] - human	gblAAA30 846.1	69%	1023	1415
HOFC33	806819	821	HMMER 2.1.1 WUblastx.64	PFAM: 60s Acidic ribosomal protein acidic ribosomal protein P0, cytosolic [validated] - human	gblAAA30 846.1	81%	115	432
HOFC33	806819	821	HMMER 2.1.1 WUblastx.64	PFAM: 60s Acidic ribosomal protein acidic ribosomal protein P0, cytosolic [validated] - human	PF00428	74.6	-422	-733
HOFC33	806819	821	HMMER 2.1.1 WUblastx.64	PFAM: 60s Acidic ribosomal protein acidic ribosomal protein P0, cytosolic [validated] - human	pirA2712 5[R5HUP0	52%	5	55
HOFC33	806819	821	HMMER 2.1.1 WUblastx.64	PFAM: 60s Acidic ribosomal protein acidic ribosomal protein P0, cytosolic [validated] - human	pirA2712 5[R5HUP0	87%	42	812

HOF0C73	931871	433	HMMER 2.1.1 WUblastx.64	PFAM: Papain family cysteine protease (BAB22302) Adult male kidney cDNA, RIKEN full-length	PF00112 BAB2230 2	22.3 71% 87%	192 72 316	311 341 918
HOGAW62	579891	434	WUblastx.64	(AAH20830) Hypothetical 19.2 kDa protein.	AAH2083 0	100%	35	130
HOGCK20	745445	435	WUblastx.64	(Q969N2) Phosphatidyl inositol glycan class T precursor (Hypothetical)	Q969N2	99% 97%	378 57	1622 389
HOGCK63	895880	436	WUblastx.64	(Q9Y386) CGI-78 PROTEIN.	Q9Y386	69% 88% 92%	1214 1161 514	1252 1214 1161
HOGCK63	902295	826	WUblastx.64	(Q96BI3) Hypothetical 29.0 kDa protein.	Q96BI3	100% 96%	813 22	872 477
HOGCS52	919898	437	WUblastx.64	(Q9NY68) CTL2 PROTEIN.	Q9NY68	90%	79	1383
HOHBB49	833080	438	WUblastx.64	(Q96MM0) CDNA FLJ32172 fis, clone PLACE600055.	Q96MM0	57%	2582	2292
HOHBC68	603968	439	WUblastx.64	(AAH20256) Hypothetical 110.4 kDa protein.	AAH2025 6	94% 97%	348 676	707 1785
HOHBY44	873264	441	WUblastx.64	(O60565) GREMLIN (DRM).	O60565	83%	170	721
HOHCH55	827481	443	WUblastx.64	(O95965) TEN INTEGRIN EGF-LIKE REPEAT DOMAINS PROTEIN PRECURSOR.	O95965	84%	221	1702
HOHCH55	815682	831	blastx.2	(AF072752) ten integrin EGF-like repeat domains protein precursor [Homo sapiens]	gb AAD17666.1	99% 42% 35% 100%	230 326 416 1623	1621 1426 1576 1712
HONAH29	1299928	444	WUblastx.64	(Q9NWM8) CDNA FLJ20731 FIS, CLONE HEP10272 (HYPOTHETICAL 24.2 KDA PRO	Q9NWM8	93%	136	768
HONAH29	457167	832	HMMER 2.1.1	PFAM: FKBP-type peptidyl-prolyl cis-trans isomerases	PF00254	95.1	288	539
			WUblastx.64	(Q9NWM8) CDNA FLJ20731 FIS, CLONE HEP10272 (HYPOTHETICAL 24.2 KDA PRO	Q9NWM8	98%	144	776
HOSDJ25	854234	445	WUblastx.64	(Q9D8Y9) 1810018L05RIK PROTEIN.	Q9D8Y9	85% 86%	468 143	593 544
HOSEG51	545809	446	WUblastx.64	(Q9NUT5) CDNA FLJ11152 FIS, CLONE	Q9NUT5	51%	2	82

HOSFD58	614040	447	HMMER 2.1.1 WUblastx.64	PLACE1006901 (FRAGMENT). PFAM: ATP-sulfurylase 3'-phosphoadenosine-5'-phosphosulfate synthetase - human	PF01747 pirJW008 7JW0087	100% 697.3 100%	46 -647 56	537 -1633 1927
HOUQC17	429229	448	HMMER 2.1.1 WUblastx.64	PFAM: Reprolysin family propeptide (P97857) ADAM-TS 1 PRECURSOR (EC 3.4.24.-) (A DISINTEGRIN A (Q9NUX1) CDNA FLJ11082 FIS, CLONE PLACE1005206.	PF01562 ATSI_M OUSE	76.2 81%	216 508	-20 3408
HOUDK26	565393	449	WUblastx.64	(Q9NUX1) CDNA FLJ11082 FIS, CLONE PLACE1005206.	Q9NUX1	94%	4	585
HPASA81	900548	835	HMMER 2.1.1 WUblastx.64	PFAM: CUB domain (O35360) UTERUS-OVARY SPECIFIC PUTATIVE TRANSMEMBRANE PROTEIN.	PF00431 O35360	146.9 70% 75%	452 8 918	778 928 1814
HPASA81	801923	836	blastx.2	(AF022147) uterus-ovary specific putative transmembrane protein [Rattus norvegicus]	gb AAB71 895.1	69% 60% 33% 40%	299 106 641 1009	1924 333 934 1119
HPBCU51	411080	452	WUblastx.64	(Q9BWJ9) SIMILAR TO NEUROBLASTOMA (NERVE TISSUE) PROTEIN.	Q9BWJ9	96%	56	154
HPFCL43	535710	457	WUblastx.64	(AAH07349) Adrenal gland protein AD-004.	AAH0734 9	97%	57	257
HPFDG48	542227	458	WUblastx.64	(Q9Y6E5) HSPC024-ISO.	Q9Y6E5	90% 88%	564 313	623 387
HPLAQ68	833082	459	WUblastx.64	(Q95LL4) Hypothetical 13.9 kDa protein.	Q95LL4	46%	905	1174
HPIBO15	1310868	460	WUblastx.64	(Q9CQS3) 1110018M03RIK PROTEIN.	Q9CQS3	93%	128	757
HPIBO15	590741	839	WUblastx.64	(Q9CQS3) 1110018M03RIK PROTEIN.	Q9CQS3	88% 95% 97%	127 507 401	402 722 508
HPICB53	1042309	461	WUblastx.64	(Q96LS9) CDNA FLJ25101 fis, clone CBR01328.	Q96LS9	66%	1124	849
HPJCL22	1146674	463	WUblastx.64	(Q9GKV3) HYPOTHETICAL 41.8 KDA PROTEIN.	Q9GKV3	92% 75%	1540 2701	2508 2823
HPJCL22	1034817	844	blastx.2	cDNA EST EMBL:M89462 comes from this gene; cDNA EST 11 yk349d7.5 comes from this gene; cDNA EST yk358b9.5 comes from this	emb CAA 94301.1	44% 29%	534 94	896 345

HPJCL22	1046434	845	blastx.2	(AK000385) unnamed protein product [Homo sapiens]	dbj BAA91131.1	71%	705	568
HPICW04	589969	464	WUblastx.64	(Q9N083) UNNAMED PORTEIN PRODUCT.	Q9N083	66%	743	702
HPMAI22	635491	466	WUblastx.64	(Q9CX19) 9430073N08RIK PROTEIN.	Q9CX19	45%	1275	1144
HPQAC69	396804	469	WUblastx.64	(O75592) PROTEIN ASSOCIATED WITH MYC.	O75592	54%	1450	1265
HPRBC80	829136	470	HMMER 2.1.1	(Q9CX19) 9430073N08RIK PROTEIN.	Q9CX19	65%	147	629
			WUblastx.64	(O75592) PROTEIN ASSOCIATED WITH MYC.	O75592	100%	202	297
HPRBF19	733282	471	WUblastx.64	(Q9H817) CDNA FLJ13593 FIS, CLONE PLACE1009493.	Q9H817	28%	76	189
HPTVX32	634353	473	WUblastx.64	(Q9H817) CDNA FLJ13593 FIS, CLONE PLACE1009493.	Q9H817	100%	3	200
HPWDJ42	722246	476	WUblastx.64	(Q9HD20) CGI-152 PROTEIN.	Q9HD20	336.4	157	957
HPZAB47	585702	477	WUblastx.64	(Q9H728) CDNA: FLJ21463 FIS, CLONE COL04765.	Q9H728	97%	94	1254
HRAAB15	658717	478	WUblastx.64	hypothetical protein 3 - human	Q9H728	99%	15	632
HRABA80	882176	479	WUblastx.64	(Q9BVS2) UNKNOWN (PROTEIN FOR IMAGE:3451448) (FRAGMENT).	Q9BVS2	86%	103	231
HRABA80	588460	855	WUblastx.64	(Q9HA75) CDNA FLJ12122 FIS, CLONE MAMMA1000129.	Q9HA75	98%	303	557
HRACD15	871221	480	WUblastx.64	(Q9HA75) CDNA FLJ12122 FIS, CLONE MAMMA1000129.	Q9HA75	64%	1100	1026
HRACD80	1309774	481	WUblastx.64	(AAH08084) Hypothetical 50.4 kDa protein.	AAH08084	67%	1332	1102
				(CAC37630) Fibulin-6 (Fragment).	CAC37630	34%	1132	884
						55%	1296	1183
						40%	14	511
						63%	221	310
						68%	325	459
						63%	633	665
						48%	130	357
						92%	233	493
						98%	1452	253
						44%	700	1866
						36%	37	1446
						45%	1282	1920
						42%	1291	1584
						47%	1291	1530

HRACD80	882163	857	HMMER 2.1.1 WUblastx.64	PFAM: EGF-like domain (CAC37630) Fibulin-6 (Fragment).	PF00008 CAC3763 0	64.3 44% 37% 45% 42% 47% 28% 33%	1337 695 32 1277 1286 1286 1839 285	1441 1861 1441 1915 1579 1525 1913 440
HRACD80	740762	858	blastx.2	(AF135253) fibulin-2 [Mus musculus]	gb AAD34 456.1	33% 31% 45% 49% 44% 30% 43% 31% 43% 35% 41% 42% 41% 48% 43% 33% 36% 30% 33% 37% 43% 46% 28% 33% 26% 31%	898 1279 1279 681 898 901 928 802 699 690 928 699 699 699 1339 898 540 699 699 777 925 898 493 576 952	1581 1893 1608 911 1125 1605 1149 1137 899 998 1119 911 908 890 914 1533 1137 995 893 890 899 1002 1065 609 890 1125

HRDDV47	637650	482	WUblastx.64	(Q9VXD6) CG9723 PROTEIN.	Q9VXD6	27%	807	1061
HRDFD27	567004	483	WUblastx.64	(Q9N032) UNNAMED PROTEIN PRODUCT.	Q9N032	36%	943	1041
HROAJ03	567005	484	WUblastx.64	(Q96A82) CDNA FLJ30106 fis, clone BNGH41000190, weakly similar to Rat	Q96A82	24%	699	869
HSATR82	531973	486	WUblastx.64	(Q9UI58) PRO0483 PROTEIN.	Q9UI58	23%	1057	1218
HSAUL82	490879	488	WUblastx.64	(Q9BE22) HYPOTHETICAL 13.4 KDA PROTEIN.	Q9BE22	70%	1066	1095
HSAVH65	545459	489	WUblastx.64	(Q9CZR4) 2700018N07RIK PROTEIN.	Q9CZR4	35%	928	1053
HSAVK10	561435	490	WUblastx.64	(Q9H728) CDNA: FLJ21463 FIS, CLONE COL04765.	Q9H728	27%	83	964
HSAWD74	460527	491	WUblastx.64	(Q9NX85) CDNA FLJ20378 FIS, CLONE KALA0536.	Q9NX85	47%	679	476
HSAWZ41	580872	492	WUblastx.64	(Q9H387) PRO2550.	Q9H387	88%	7	786
HSAXA83	545051	493	WUblastx.64	(Q9NRX6) PROTEIN X 013.	Q9NRX6	80%	678	707
HSAYB43	604143	494	WUblastx.64	(Q9N083) UNNAMED PORTEIN PRODUCT.	Q9N083	76%	605	682
HSDAJ46	692358	496	HMMER 2.1.1	PFAM: Eukaryotic-type carbonic anhydrase	PF00194	63%	546	701
			WUblastx.64	(Q9ULX7) CARBONIC ANHYDRASE XIV PRECURSOR (EC 4.2.1.1) (CAR	CAHE_H UMAN	92%	23	403
HSDEK49	625998	861	HMMER 2.1.1	PFAM: Immunoglobulin domain	PF00047	70%	1055	933
			WUblastx.64	(Q9Y279) Z39IG PROTEIN PRECURSOR.	Q9Y279	63%	1218	1030
HSDEZ20	1352287	499	blastx.14	probable voltage-activated cation channel - rat	pir T1710 1 T17101	67%	967	674
HSDEZ20	704101	862	WUblastx.64	probable voltage-activated cation channel - rat	pir T1710 1 T17101	81%	1386	1102
HSDFW45	589974	500	WUblastx.64	(Q9NX85) CDNA FLJ20378 FIS, CLONE	Q9NX85	100%	92	313
						60%	1662	1573
						50%	1580	1338
						163.5	362	793
						99%	299	796
						98%	791	1084
						18.7	225	470
						88%	444	1040
						99%	126	542
						89%	4	336
						60%	705	734
						89%	9	335
						77%	1645	1352

HSDJA15	795252	501	WUblastx.64	KAIA0536. (Q9BZW5) TRANSMEMBRANE 6 SUPERFAMILY MEMBER 1.	Q9BZW5	99%	4	702
HSDJL42	1036471	503	WUblastx.64	(Q9BVS2) UNKNOWN (PROTEIN FOR IMAGE:3451448) (FRAGMENT).	Q9BVS2	54%	57	590
HSDJL42	904821	863	blastx.2	(AC021665) unknown protein [Arabidopsis thaliana]	gb AAF34 307.1	39%	6	515
HSDSE75	545057	506	WUblastx.64	(Q60245) PCDH7 (BH-PCDH)A.	Q60245	100%	10	702
HSDZR57	651375	507	WUblastx.64	(Q9NX00) CDNA FLJ20512 FIS, CLONE KAT09739.	Q9NX00	100%	9	209
HSHAX21	612823	508	WUblastx.64	(Q9NV22) CDNA FLJ10983 FIS, CLONE PLACE1001781, WEAKLY SIMILAR TO PRO	Q9NV22	99%	5	598
HSIAS17	514183	866	WUblastx.64	(Q9H6H4) CDNA: FLJ22277 FIS, CLONE HRC03740.	Q9H6H4	100% 88%	108 350	362 877
HSICV24	612877	867	WUblastx.64	(Q96J88) Putative breast epithelial stromal interaction protein.	Q96J88	100%	251	916
HSID181	589447	511	WUblastx.64	(Q9H728) CDNA: FLJ21463 FIS, CLONE COL04765.	Q9H728	74%	1289	996
HSIDX71	1033671	512	WUblastx.64	(AAK55521) PRO0764.	AAK5552 1	59% 65%	1829 1786	1764 1526
HSJBQ79	1304677	513	WUblastx.64	(Q96D15) Hypothetical 37.5 kDa protein.	Q96D15	96%	38	586
HSJBQ79	661698	869	HMMER 2.1.1	PFAM: EF hand	PF00036	23.4	663	734
			WUblastx.64	(Q96D15) Hypothetical 37.5 kDa protein.	Q96D15	99%	54	1037
HSKCP69	702021	514	WUblastx.64	(Q9H5G5) CDNA: FLJ23462 FIS, CLONE HSI08475.	Q9H5G5	99%	49	906
HSKDA27	1074734	872	WUblastx.64	(Q9CRM1) 2610001E17RIK PROTEIN (FRAGMENT).	Q9CRM1	70% 60% 23%	793 1686 1604	1701 1784 1741
HSKDA27	872570	873	blastx.2	(AK020169) putative [Mus musculus]	dbj BAB3 2018.1	47%	666	1562
HSQEO84	1306702	522	WUblastx.64	(Q9Y6B0) FK506-BINDING PROTEIN.	Q9Y6B0	99%	75	740
HSQEO84	602258	879	HMMER 2.1.1	PFAM: FKBP-type peptidyl-prolyl cis-trans isomerases	PF00254	92	-30	-326

HSSDX51	566879	524	WUblastx.64	(Q96DA4) FK506-binding protein. (Q9NQ80) ASPIC PRECURSOR.	Q96DA4 Q9NQ80	100% 83% 40% 72% 41% 32% 26% 92%	79 15 301 10 174 78 99 323	744 368 399 69 266 251 257 1105
HSSGD52	845666	881	WUblastx.64	(Q96FI8) Unknown (protein for MGC:9160).	Q96FI8	100%	338	2155
HSSJC35	1306937	528	WUblastx.64	(Q9H400) DJ583P15.4.1 (NOVEL PROTEIN (TRANSLATION OF CDNA FLJ20406 (E	Q9H400	81%	62	946
HSSJC35	745409	882	WUblastx.64	(Q9H400) DJ583P15.4.1 (NOVEL PROTEIN (TRANSLATION OF CDNA FLJ20406 (E	Q9H400	100%	55	939
HSUBW09	413246	530	WUblastx.64	(Q95LL0) Hypothetical 11.3 kDa protein.	Q95LL0	73% 77%	589 327	633 611
HSVBU91	596868	533	WUblastx.64	cytoplasmic linker protein CLIP-115 - rat	pir T4273 4 T42734	85%	356	171
HSXCG83	944388	534	WUblastx.64	(Q9H7F4) CDNA: FLJ20979 FIS, CLONE ADSU01938.	Q9H7F4	99%	101	901
HSXCG83	830673	884	blastx.2	(AL117204) Y116A8C.9 [Caenorhabditis elegans]	emb CAB 55145.1	36%	10	657
HSXGI47	886200	536	WUblastx.64	(Q9H387) PRO2550.	Q9H387	52% 61% 61% 50% 72%	424 587 849 803 663	480 670 965 850 839
HSYAV50	847358	537	HMMER 2.1.1 WUblastx.64	PFAM: Leucine Rich Repeat (Q96CX1) Similar to RIKEN cDNA 2610528G05 gene (Fragment).	PF00560 Q96CX1	97.9% 96%	383 371	454 2170
HSYAZ63	1177537	540	WUblastx.64	(Q9Y613) FH1/FH2 DOMAINS-CONTAINING PROTEIN (FORMIN HOMOLOG	FHOS_H UMAN	98% 96% 93% 55%	478 2573 2101 272	1713 2941 2514 544

HSYAZ63	862063	890	WUblastx.64	(Q9Y613) FHI/FH2 DOMAINS-CONTAINING PROTEIN (FORMIN HOMOLOG	FHOS_H UMAN	33%	790	933
						33%	2030	2119
						92%	3007	3090
						28%	1015	1458
						28%	289	654
						42%	608	670
						56%	2005	2052
						41%	2220	2321
						41%	2142	2255
						37%	2098	2184
						36%	2916	3005
						42%	2913	2990
						33%	2946	3026
						69%	1756	1794
HSYBG37	1056317	541	WUblastx.64	hypothetical protein c316G12.3 [imported] - human	pirT4506 2T45062	78%	458	871
						33%	387	476
						92%	1364	1447
						100%	14	70
						96%	930	1298
						69%	113	151
						47%	558	620
						36%	561	707
						52%	362	418
						32%	455	601
						100%	122	961
HSYBG37	581098	891	WUblastx.64	hypothetical protein c316G12.3 [imported] - human	pirT4506 2T45062	100%	48	962
						54.4	299	478
HSZAF47	456551	892	HMMER 2.1.1 WUblastx.64	PFAM: Collagen triple helix repeat (20 copies) (Q9BXJ2) COMPLEMENT-C1Q TUMOR NECROSIS FACTOR-RELATED PROTEIN.	PF01391 Q9BXJ2	88%	500	976
						62%	107	397
						58%	344	394
						50%	344	397

HT3SE53	884170	543	WUblastx.64		(Q9H5B4) DJ470L14.2.1 (STAUFEN (RNA BINDING PROTEIN) ISOFORM 1).	Q9H5B4	57%	353	394
HT5GJ57	1299921	544	WUblastx.64		(Q9GZY6) CDNA FLJ11237 FIS, CLONE PLACE1008531 (WBSCR5) (WBSCR15 PROT (Q9NZY9) HSPC046.	Q9GZY6	89%	105	833
HT5GJ57	740767	893	WUblastx.64			Q9NZY9	90%	754	1002
HTADW91	844835	545	WUblastx.64		(AAH08853) Similar to RIKEN cDNA 1100001L14 gene (F	AAH08853	70%	122	799
HTADX17	753289	546	WUblastx.64		(Q96A28) CD84-H1 (CD2 FAMILY Y 10).	Q96A28	97%	8	1150
HTADX17	457172	894	WUblastx.64		(Q96A28) CD84-H1 (CD2 FAMILY Y 10).	Q96A28	93%	92	412
HTAEE28	1018291	547	WUblastx.64		(Q9D4I2) 4932408F18RIK PROTEIN.	Q9D4I2	79%	408	959
HTDAF28	396835	548	WUblastx.64		(Q9BX79) STRA6 ISOFORM 1.	Q9BX79	78%	490	585
HTEAF65	866485	549	WUblastx.64		(Q9DAC0) 1700013O04RIK PROTEIN.	Q9DAC0	97%	548	952
HTEBI28	462221	550	WUblastx.64		(Q95LI0) Epididymis-specific protein ESP13.6.	Q95LI0	99%	84	488
HTEDF80	587326	551	WUblastx.64		(Q9NP89) HYPOTHETICAL 42.7 KDA PROTEIN (FRAGMENT).	Q9NP89	72%	319	1161
HTEDY42	519372	897	HMMER 2.1.1		PFAM: SCP-like extracellular protein	PF00188	98%	17	298
			WUblastx.64		(Q96L06) Similar to RIKEN cDNA 1700011E04 gene.	Q96L06	44%	9	287
HTEGI42	908143	555	WUblastx.64		(AAH20905) Hypothetical 28.5 kDa protein.	AAH20905	46%	43	231
HTEHR24	835894	556	WUblastx.64		(Q9HBV2) SPERM MEMBRANE ANTIGEN SMARC32.	Q9HBV2	100%	253	327
							30%	1016	1135
							100%	852	1073
							75%	112	210
							98%	698	856
							91%	353	451
							66%	450	863
							20	-98	-193
							100%	19	231
							33%	576	719
							94%	224	700
							88%	41	796
							76%	84	959

HTEHR24	513039	902	WUblastx.64	(Q9HBV2) SPERM MEMBRANE ANTIGEN SMARC32.	Q9HBV2	76%	41	529
HTEHU93	722254	557	WUblastx.64	(O60676) CYSTATIN-RELATED EPIDIDYMAL SPERMATOGENIC PROTEIN	*CRES_H UMAN	100%	692	922
HTEHU93	423009	903	HMMER 2.1.1 WUblastx.64	PFAM: Cystatin domain	PF00031	96%	514	693
				(O60676) CYSTATIN-RELATED EPIDIDYMAL SPERMATOGENIC PROTEIN	CRES_H UMAN	91%	188	613
HTEIN13	658744	904	WUblastx.64	(Q9DAR9) 1700001D09RIK PROTEIN.	Q9DAR9	31.7	35	-105
HTEPG70	834931	562	WUblastx.64	(O75295) R27328.2.	O75295	100%	504	614
HTGAU75	597467	563	WUblastx.64	(Q9NZX5) HSPC062.	Q9NZX5	78%	187	552
HTGEP89	410582	564	WUblastx.64	(Q9DAL9) 1700007K09RIK PROTEIN.	Q9DAL9	60%	525	743
HTHBG43	919911	565	WUblastx.64	(Q9H387) PRO2550.	Q9H387	77%	163	516
HTHDJ94	693652	567	HMMER 2.1.1 WUblastx.64	PFAM: Oxidoreductase FAD/NAD-binding domain (Q9UHQ9) NADH-CYTOCHROME B5 REDUCTASE ISOFORM.	PF00175 Q9UHQ9	93%	23	268
				(Q9P1H3) PRO1438.	Q9P1H3	55%	502	672
HTHDS25	772559	568	WUblastx.64	PFAM: Ammonium Transporter Family	PF00909	72%	149	661
HTJMA95	706618	569	HMMER 2.1.1 WUblastx.64	(Q9UBD6) RH TYPE C GLYCOPROTEIN (TUMOR-RELATED PROTEIN DRC2).	Q9UBD6	44%	258	566
				(Q9UJX6) ANAPHASE-PROMOTING COMPLEX SUBUNIT 2.	Q9UJX6	83%	772	701
HTJML75	1040047	570	WUblastx.64	(Q9UJX6) ANAPHASE-PROMOTING COMPLEX SUBUNIT 2.	Q9UJX6	70%	702	571
HTJML75	873355	908	WUblastx.64	(Q9UJX6) ANAPHASE-PROMOTING COMPLEX SUBUNIT 2.	Q9UJX6	160.3	552	896
				(Q9NV11) CDNA FLJ11004 FIS, CLONE PLACE1002941.	Q9NV11	95%	66	941
HTLAA40	519329	571	WUblastx.64	(Q96M29) CDNA FLJ32871 fis, clone TEST12003914, weakly similar to Tek	Q96M29	66%	1045	911
HTLBE23	902187	572	WUblastx.64			62.1	533	691
						98%	3	455
						100%	449	1069
						94%	30	2495
						78%	40	423
						94%	423	1016
						89%	911	2503
						100%	360	482
						100%	14	217
						98%	176	838
						93%	840	980
						81%	1112	1177

HTLEP53	634852	573	WUblastx.64	(Q9H728) CDNA: FLJ121463 FIS, CLONE COL04765.	Q9H728	69%	806	501
HTLFE42	460583	574	WUblastx.64	(Q9NSI0) PRED58 PROTEIN (FRAGMENT).	Q9NSI0	99%	17	346
HTLFE57	791409	910	WUblastx.64	(Q9D7G6) 2310009N05RIK PROTEIN.	Q9D7G6	90%	12	698
HTLFE57	608317	911	WUblastx.64	(Q9D7G6) 2310009N05RIK PROTEIN.	Q9D7G6	84%	2	619
HTLGE31	1035130	576	WUblastx.64	(Q9NY64) GLUCOSE TRANSPORTER.	Q9NY64	100%	3	92
HTLHY14	838460	577	WUblastx.64	(Q96L02) Hypothetical 24.5 kDa protein.	Q96L02	99%	36	434
						100%	528	773
HTLIT32	833906	578	WUblastx.64	(Q96QH1) NB1 Glycoprotein precursor.	Q96QH1	32%	312	932
						29%	330	1007
HTLIV19	1046341	579	WUblastx.64	(Q96LS9) CDNA FLJ25101 fis, clone CBR01328.	Q96LS9	73%	193	315
HTODK73	526021	582	WUblastx.64	(Q9H8P2) CDNA FLJ13348 FIS, CLONE OVARC1002127, WEAKLY SIMILAR TO SOD	Q9H8P2	93%	404	448
						100%	567	707
						71%	433	474
						43%	4	189
						61%	418	519
						80%	21	401
HTOIM15	1028538	585	WUblastx.64	(Q9NVL9) CDNA FLJ10649 FIS, CLONE NT2RP2005835, WEAKLY SIMILAR TO SHP	Q9NVL9	96%	1641	1718
HTOIM15	848200	914	HMMER 2.1.1	PFAM: UBX domain	PF00789	97.6	794	1033
HTOJA73	797108	589	WUblastx.64	(Q9H387) PRO2550.	Q9H387	63%	1044	955
						66%	1294	1046
HTOJK60	545067	590	WUblastx.64	(Q9HA67) CDNA FLJ12155 FIS, CLONE MAMMA1000472.	Q9HA67	73%	745	644
						78%	870	757
HTPBW79	1317835	591	WUblastx.64	(Q9CXR7) 3110023E09RIK PROTEIN.	Q9CXR7	77%	172	813
						92%	787	999
HTPBW79	581435	917	WUblastx.64	(Q96S93) Hypothetical 41.7 kDa protein.	Q96S93	95%	302	1387
HTTDB46	812763	593	WUblastx.64	(Q9Y2C7) BUTYROPHILIN LIKE RECEPTOR.	Q9Y2C7	70%	106	543
						83%	727	762
						59%	1007	1072
						100%	1644	2180
HTTDB46	909573	919	HMMER 2.1.1	PFAM: SPRY domain	PF00622	65.9	-956	-1276
HTWCT03	429618	594	WUblastx.64	(Q95014) WUGSC:H_DJ0855D21.2 PROTEIN.	O95014	82%	1488	1592

HTWDF76	714344	595	WUblastx.64	(Q9BTF2) REC8P, A MEIOTIC RECOMBINATION AND SISTER CHROMATID COHESION	Q9BTF2	100%	792	875
HTXAJ12	1310814	596	WUblastx.64	(Q9D7W4) 2210021G2IRIK PROTEIN.	Q9D7W4	45%	12	77
HTXAJ12	567434	920	WUblastx.64	(Q9D7W4) 2210021G2IRIK PROTEIN.	Q9D7W4	45%	12	77
HTXDW56	695765	598	WUblastx.64	(Q96A54) Similar to CGI-45 protein (Hypothetical 42.6 kDa protein).	Q96A54	99%	7	819
HTXFL30	620001	599	WUblastx.64	(Q96KR5) Leishmanolysin-like peptidase, variant 2 (EC 3.4.24.36).	Q96KR5	98%	305	1990
HTXKF95	891275	600	WUblastx.64	(AAH08360) Similar to hypothetical protein FLJ22376	AAH08360	97%	81	644
HTXKF95	834438	922	WUblastx.64	(AAH08360) Similar to hypothetical protein FLJ22376	AAH08360	85%	233	553
HTXKP61	824083	601	WUblastx.64	(Q9H0S8) HYPOTHETICAL 53.0 KDA PROTEIN.	Q9H0S8	100%	2	112
HUDBZ89	562791	923	WUblastx.64	(Q9VH80) CG16908 PROTEIN.	Q9VH80	98%	3	1124
HUFEF62	645101	604	WUblastx.64	hypothetical L1 protein (third intron of gene TS) - human	Q9VH80	22%	7	327
HUKAH51	1300737	926	WUblastx.64	(Q9ES75) PROLINE-RICH ACIDIC PROTEIN.	Q9ES75	33%	330	641
HUKAH51	603538	927	WUblastx.64	(Q96NZ9) Proline-rich acidic protein.	Q96NZ9	81%	355	308
HUKBT29	694590	606	WUblastx.64	(Q96AA2) Obscurin.	Q96AA2	84%	314	12
						50%	144	563
						100%	462	479
						93%	55	462
						82%	131	1300
						30%	520	597
						33%	500	571

HUSIG64	566762	607	WUblastx.64	(O60763) GENERAL VESICULAR TRANSPORT FACTOR P115 (TRANSCYTO	VDP_HU MAN	29%	152	370
HUSXS50	883176	928	WUblastx.64	(AAH08361) F-box only protein 7.	AAH0836 1	99%	1039	1338
HUSXS50	655372	929	WUblastx.64	(AAH08361) F-box only protein 7.	AAH0836 1	42%	597	710
HWAAD63	838626	610	HMMER 2.1.1 WUblastx.64	PFAM: Sodium/calcium exchanger protein (Q9HC58) SODIUM/CALCIUM EXCHANGER NCKX3.	PF01699 Q9HC58	100%	134	316
HWAAD63	833089	931	HMMER 2.1.1 blastx.2	PFAM: Sodium/calcium exchanger protein (AF177984) potassium-dependent sodium-calcium exchanger NCKX1 [Gallus gallus]	PF01699 gb AAF25 808.1 AF1 77984_1	77%	9	1010
HWAAD63	793875	932	HMMER 2.1.1 blastx.2	PFAM: Sodium/calcium exchanger protein (AF025664) Na-Ca+K exchanger [Bos taurus]	PF01699 gb AAB88 884.1	26%	281	1069
HWABY10	768334	612	WUblastx.64	(Q96AW1) Hypothetical 19.2 kDa protein.	Q96AW1	43%	1566	1622
HWBAO62	838164	614	HMMER 2.1.1 WUblastx.64	PFAM: Immunoglobulin domain (Q14288) HYPOTHETICAL PROTEIN (FRAGMENT).	PF00047 Q14288	100%	1067	1666
HWBAR88	836469	615	WUblastx.64	(Q9Y2C2) DERMATAN/CHONDROITIN SULFATE 2-SULFOTRANSFERASE.	Q9Y2C2	45%	958	1050
HWBCB89	1093347	616	WUblastx.64	(BAB55294) CDNA FLJ14777 fis, clone	BAB5529	66%	107	241
						62%	215	982
						55%	94	576

HWBCB89	886210	934	HMMER 2.1.1	NT2RP4000259, w	4	PF00255	170.2	104	433
			WUblastx.64	PFAM: Glutathione peroxidases (BAB55294) CDNA FLJ14777 fis, clone NT2RP4000259, w	4	BAB5529	100%	35	595
HWBCP79	846382	617	WUblastx.64	(AAH20829) Hypothetical 6.2 kDa protein.	9	AAH2082	78%	134	93
HWBCP79	646977	935	WUblastx.64	(Q96MM0) CDNA FLJ32172 fis, clone PLACE6000555.	9	Q96MM0	78%	72	16
HWBFES7	907063	619	WUblastx.64	(Q9NR73) MACROPHAGE ABC TRANSPORTER.	9	Q9NR73	27%	330	133
HWDAH38	1028519	621	WUblastx.64	(Q9NX85) CDNA FLJ20378 FIS, CLONE KAIA0536.	9	Q9NX85	85%	148	68
HWHGP71	995431	622	HMMER 2.1.1	PFAM: 7 transmembrane receptor (rhodopsin family)	9	PF00001	78%	206	1048
			WUblastx.64	leukotriene B4 receptor 2, BLTR2 - human	9	pirJC7356 JC7356	69%	1113	1250
					9		63%	979	1119
					9		81%	947	979
					9		52%	1534	1340
					9		60%	1602	1528
HWHGP71	839250	941	blastx.2	(AJ278605) leukotriene B4 receptor 2 [Homo sapiens]	9	emb CAB 96134.1	31.2	389	766
HWHGQ49	636080	942	WUblastx.64	(Q9Y5B4) ANDROGEN INDUCED PROTEIN.	9	Q9Y5B4	94%	101	766
HWHGU54	695695	624	HMMER 2.1.1	PFAM: Serpins (serine protease inhibitors)	9	PF00079	35%	487	591
			WUblastx.64	(Q9CQ32) 4632419I12RIK PROTEIN.	9	Q9CQ32	47%	434	484
HWHGZ51	886212	625	WUblastx.64	(Q9UJ74) HYPOTHETICAL 36.0 KDA PROTEIN (C4.4A PROTEIN).	9	Q9UJ74	84%	715	1020
					9		77%	106	465
HWHHL34	805642	626	WUblastx.64	(O75915) JWA PROTEIN (HSPC127) (VITAMIN A RESPONSIVE, CYTOSKELETON RE	9	O75915	100%	555	770
HWHHL34	801943	943	blastx.2	(AF070523) JWA protein [Homo sapiens]	9	gb AAC64 360.1	58%	776	1036
					9		99%	42	755
					9		501.1	277	1377
					9		61%	145	1383
					9		86%	33	1022
					9		100%	131	694
					9		92%	53	613

HWLEV32	846351	947	WUblastx.64	(Q9W6Q6) OSTEOLAST 6D12C PROTEIN.	Q9W6Q6	88%	143	421
HWLIH65	793713	628	HMMER 2.1.1	PFAM: Integral membrane protein	PF01940	49.3	147	455
			WUblastx.64	(AAH08596) Unknown (protein for MGC:16985).	AAH08596	98%	81	623
HYAAJ71	826754	630	WUblastx.64	(Q9NX17) CDNA FLJ20489 FIS, CLONE KAT08285.	Q9NX17	62%	1147	1464

RACE Protocol For Recovery of Full-Length Genes

Partial cDNA clones can be made full-length by utilizing the rapid amplification of cDNA ends (RACE) procedure described in Frohman, M.A., et al., Proc. Nat'l. Acad. Sci. USA, 85:8998-9002 (1988). A cDNA clone missing either the 5' or 3' end can be reconstructed to include the absent base pairs extending to the translational start or stop codon, respectively. In some cases, cDNAs are missing the start codon of translation, therefor. The following briefly describes a modification of this original 5' RACE procedure. Poly A+ or total RNA is reverse transcribed with Superscript II (Gibco/BRL) and an antisense or complementary primer specific to the cDNA sequence. The primer is removed from the reaction with a Microcon Concentrator (Amicon). The first-strand cDNA is then tailed with dATP and terminal deoxynucleotide transferase (Gibco/BRL). Thus, an anchor sequence is produced which is needed for PCR amplification. The second strand is synthesized from the dA-tail in PCR buffer, Taq DNA polymerase (Perkin-Elmer Cetus), an oligo-dT primer containing three adjacent restriction sites (XhoI, SalI and ClaI) at the 5' end and a primer containing just these restriction sites. This double-stranded cDNA is PCR amplified for 40 cycles with the same primers as well as a nested cDNA-specific antisense primer. The PCR products are size-separated on an ethidium bromide-agarose gel and the region of gel containing cDNA products the predicted size of missing protein-coding DNA is removed. cDNA is purified from the agarose with the Magic PCR Prep kit (Promega), restriction digested with XhoI or SalI, and ligated to a plasmid such as pBluescript SKII (Stratagene) at XhoI and EcoRV sites. This DNA is transformed into bacteria and the plasmid clones sequenced to identify the correct protein-coding inserts. Correct 5' ends are confirmed by comparing this sequence with the putatively identified homologue and overlap with the partial cDNA clone. Similar methods known in the art and/or commercial kits are used to amplify and recover 3' ends.

Several quality-controlled kits are commercially available for purchase. Similar reagents and methods to those above are supplied in kit form from Gibco/BRL for both 5' and 3' RACE for recovery of full length genes. A second kit is available from Clontech which is a modification of a related technique, SLIC (single-stranded ligation to single-stranded cDNA), developed by Dumas et al., Nucleic Acids Res., 19:5227-32 (1991). The major differences in procedure are that the RNA is alkaline hydrolyzed after reverse transcription and RNA ligase is used to join a restriction site-containing anchor primer to the first-strand cDNA. This obviates the necessity for the dA-tailing reaction which results in a polyT stretch that is difficult to sequence past.

An alternative to generating 5' or 3' cDNA from RNA is to use cDNA library double-stranded DNA. An asymmetric PCR-amplified antisense cDNA strand is synthesized with an antisense cDNA-specific primer and a plasmid-anchored primer. These primers are removed and a symmetric PCR reaction is performed with a nested cDNA-specific antisense primer and the plasmid-anchored primer.

RNA Ligase Protocol For Generating The 5' or 3' End Sequences To Obtain Full Length Genes

Once a gene of interest is identified, several methods are available for the identification of the 5' or 3' portions of the gene which may not be present in the original cDNA plasmid. These methods include, but are not limited to, filter probing, clone enrichment using specific probes and protocols similar and identical to 5' and 3' RACE. While the full length gene may be present in the library and can be identified by probing, a useful method for generating the 5' or 3' end is to use the existing sequence information from the original cDNA to generate the missing information. A method similar to 5' RACE is available for generating the missing 5' end of a desired full-length gene. (This method was published by Fromont-Racine et al., *Nucleic Acids Res.*, 21(7):1683-1684 (1993)). Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcript and a primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest, is used to PCR amplify the 5' portion of the desired full length gene which may then be sequenced and used to generate the full length gene. This method starts with total RNA isolated from the desired source, poly A RNA may be used but is not a prerequisite for this procedure. The RNA preparation may then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase if used is then inactivated and the RNA is treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase. This modified RNA preparation can then be used as a template for first strand cDNA synthesis using a gene specific oligonucleotide. The first strand synthesis reaction can then be used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the relevant gene.

The present invention also relates to vectors or plasmids which include such DNA sequences, as well as the use of the DNA sequences. The material deposited with the ATCC (e.g., as described in columns 2 and 3 of Table 1A, and/or as set forth in Table 1B, Table 6, or Table 7) is a mixture of cDNA clones derived from a variety of human tissue and cloned in either a plasmid vector or a phage vector, as described, for example, in Table 1A and Table 7. These deposits are referred to as "the deposits" herein. The tissues from which some of the clones were derived are listed in Table 7, and the vector in which the corresponding cDNA is contained is also indicated in Table 7. The deposited material includes cDNA clones corresponding to SEQ ID NO:X described, for example, in Table 1A and/or Table 1B (ATCC Deposit No:Z). A clone which is isolatable

from the ATCC Deposits by use of a sequence listed as SEQ ID NO:X, may include the entire coding region of a human gene or in other cases such clone may include a substantial portion of the coding region of a human gene. Furthermore, although the sequence listing may in some instances list only a portion of the DNA sequence in a clone included in the ATCC Deposits, it is well within the ability of one skilled in the art to sequence the DNA included in a clone contained in the ATCC Deposits by use of a sequence (or portion thereof) described in, for example Tables 1A and/or Table 1B or Table 2, by procedures hereinafter further described, and others apparent to those skilled in the art.

Also provided in Table 1A and Table 7 is the name of the vector which contains the cDNA clone. Each vector is routinely used in the art. The following additional information is provided for convenience.

Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., *Nucleic Acids Res.* 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., *Nucleic Acids Res.* 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., *Strategies* 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Phagemid pBS may be excised from the Lambda Zap and Uni-Zap XR vectors, and phagemid pBK may be excised from the Zap Express vector. Both phagemids may be transformed into *E. coli* strain XL-1 Blue, also available from Stratagene.

Vectors pSport1, pCMVSPORT 1.0, pCMVSPORT 2.0 and pCMVSPORT 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, also available from Life Technologies. See, for instance, Gruber, C. E., et al., *Focus* 15:59- (1993). Vector lacmid BA (Bento Soares, Columbia University, New York, NY) contains an ampicillin resistance gene and can be transformed into *E. coli* strain XL-1 Blue. Vector pCR[®]2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, available from Life Technologies. See, for instance, Clark, J. M., *Nuc. Acids Res.* 16:9677-9686 (1988) and Mead, D. et al., *Bio/Technology* 9: (1991).

The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, and/or the deposited clone (ATCC Deposit No:Z). The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

Also provided in the present invention are allelic variants, orthologs, and/or species homologs. Procedures known in the art can be used to obtain full-length genes, allelic variants,

splice variants, full-length coding portions, orthologs, and/or species homologs of genes corresponding to SEQ ID NO:X or the complement thereof, polypeptides encoded by genes corresponding to SEQ ID NO:X or the complement thereof, and/or the cDNA contained in ATCC Deposit No:Z, using information from the sequences disclosed herein or the clones deposited with the ATCC. For example, allelic variants and/or species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for allelic variants and/or the desired homologue.

The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below). It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.

The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified using techniques described herein or otherwise known in the art, such as, for example, by the one-step method described in Smith and Johnson, *Gene* 67:31-40 (1988). Polypeptides of the invention also can be purified from natural, synthetic or recombinant sources using techniques described herein or otherwise known in the art, such as, for example, antibodies of the invention raised against the polypeptides of the present invention in methods which are well known in the art.

The present invention provides a polynucleotide comprising, or alternatively consisting of, the nucleic acid sequence of SEQ ID NO:X, and/or the cDNA sequence contained in ATCC Deposit No:Z. The present invention also provides a polypeptide comprising, or alternatively, consisting of, the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X or a complement thereof, a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z, and/or the polypeptide sequence encoded by a nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1C. Polynucleotides encoding a polypeptide comprising, or alternatively consisting of the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X, a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z, and/or a polypeptide sequence encoded by a nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1C are also encompassed by the invention. The present invention further encompasses a polynucleotide comprising, or alternatively consisting of, the complement of the nucleic acid sequence of SEQ ID NO:X, a nucleic acid sequence encoding a polypeptide encoded by the

complement of the nucleic acid sequence of SEQ ID NO:X, and/or the cDNA contained in ATCC Deposit No:Z.

Moreover, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in Table 1C column 6, or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in Table 1C column 6, or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1C, column 6, and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1C, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1C, column 6, and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1C, column 6, and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

Further, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1C which correspond to the same Clone ID (see Table 1C, column 1), or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in column 6 of Table 1C which correspond to the same Clone ID (see Table 1C, column 1), or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1C which correspond to the same Clone ID (see Table 1C, column 1) and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1C, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1C which correspond to the same Clone ID (see Table 1C, column 1) and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). In additional embodiments, the above-described

polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1C which correspond to the same Clone ID (see Table 1C, column 1) and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

Further, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1C which correspond to the same contig sequence identifier SEQ ID NO:X (see Table 1C, column 2), or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in column 6 of Table 1C which correspond to the same contig sequence identifier SEQ ID NO:X (see Table 1C, column 2), or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1C which correspond to the same contig sequence identifier SEQ ID NO:X (see Table 1C, column 2) and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1C, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1C which correspond to the same contig sequence identifier SEQ ID NO:X (see Table 1C, column 2) and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1C which correspond to the same contig sequence identifier SEQ ID NO:X (see Table 1C, column 2) and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (See Table 1C, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

Moreover, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in the same row of Table 1C column 6, or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary

strand(s) of the sequences delineated in the same row of Table 1C column 6, or any combination thereof. In preferred embodiments, the polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in the same row of Table 1C column 6, wherein sequentially delineated sequences in the table (i.e. corresponding to those exons located closest to each other) are directly contiguous in a 5' to 3' orientation. In further embodiments, above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1C, column 6, and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1C, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1C, column 6, and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1C, column 6, and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1C, and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1C, column 2) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1C which correspond to the same Clone ID (see Table 1C, column 1), and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A, Table 1B, or Table 1C) or fragments or variants thereof. In preferred embodiments, the delineated sequence(s) and polynucleotide sequence of SEQ ID NO:X correspond to the same Clone ID. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in the same row of column 6 of Table 1C, and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A, Table 1B, or Table 1C) or fragments or variants thereof. In preferred embodiments, the delineated sequence(s) and polynucleotide sequence of

SEQ ID NO:X correspond to the same row of column 6 of Table 1C. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C and the 5' 10 polynucleotides of the sequence of SEQ ID NO:X are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C and the 5' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of the sequence of SEQ ID NO:X and the 5' 10 polynucleotides of the sequence of one of the sequences delineated in column 6 of Table 1C are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X and the 5' 10 polynucleotides of the sequence of one of the sequences delineated in column 6 of Table 1C are directly contiguous. Nucleic acids which

hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides, are also encompassed by the invention.

In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C and the 5' 10 polynucleotides of another sequence in column 6 are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C and the 5' 10 polynucleotides of another sequence in column 6 corresponding to the same Clone ID (see Table 1C, column 1) are directly contiguous. Nucleic acids which hybridize to the complement of these 20 lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one sequence in column 6 corresponding to the same contig sequence identifier SEQ ID NO:X (see Table 1C, column 2) are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C and the 5' 10 polynucleotides of another sequence in column 6 corresponding to the same row are directly contiguous. In preferred embodiments, the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C is directly contiguous with the 5' 10 polynucleotides of the next sequential exon delineated in Table 1C, column 6. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

Table 3

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. Accordingly, for each contig sequence (SEQ ID NO:X) listed in the fifth column of Table 1A and/or the fourth column of Table 1B, preferably excluded are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 and the final nucleotide minus 15 of SEQ ID NO:X, b is an integer of 15 to the final nucleotide of SEQ ID NO:X, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:X, and where b is greater than or equal to a + 14. More specifically, preferably excluded are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a and b are integers as defined in columns 4 and 5, respectively, of Table 3. In specific embodiments, the polynucleotides of the invention do not consist of at least one, two, three, four, five, ten, or more of the specific polynucleotide sequences referenced by the Genbank Accession No. as disclosed in column 6 of Table 3 (including for example, published sequence in connection with a particular BAC clone). In further embodiments, preferably excluded from the invention are the specific polynucleotide sequence(s) contained in the clones corresponding to at least one, two, three, four, five, ten, or more of the available material having the accession numbers identified in the sixth column of this Table (including for example, the actual sequence contained in an identified BAC clone). In no way is this listing meant to encompass all of the sequences which may be excluded by the general formula, it is just a representative example. All references available through these accessions are hereby incorporated by reference in their entirety.

Table 3

cDNA Clone ID	SEQ ID NO: X	Contig ID:	EST Disclaimer		Accession Numbers
			Range of a	Range of b	
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HADA089	18	570689	1 - 1439	15 - 1453	AA937957, AA280310, AA169289, AW474052, AV760571, AW021583, AI801482, AI281881, AA521399, AA521323, AL044940, AW970896, AV760777, AL037683, AV757607, AA587256, AW956640, BE139146, AI805363, AL042420, AI434706, AA468022, AW956641, AA502155, AV759505, AV763122, AA828704, AW276827, BF827410, AV762067, AW673241, AI564496, AA613232, AA984708, AV762571, AV761745, F03525, AV760190, AV758600, AA774780, AA507824, AA483223, AI143242, AV762535, AF330238, AC006365.3, AC021188.6, AC006509.15, AC004072.1, AL121877.13, AL133321.11, AP001748.1, AC008848.7, AC009516.19, X54181.1, U04355.1, AL109984.14, AC005197.1, AC027612.6, AL157713.10, AC002985.1, AL357497.17, AC005082.3, AL391478.14, AP002534.1, AL135839.15, AL121934.17, AC002558.1, AP000513.1, AL354735.14, AC006511.5, X54177.1, AC005081.3, Z75746.1, AC007666.12, AC006064.9, AC006019.2, AL162505.20, AL356095.11, AF205588.1, AL161670.4, AL136179.15, AC016138.8, AC004895.2, AF196779.1, AP000512.1, AC008447.7, AF117829.1, AC006464.3, X54175.1, X54178.1, AL513366.11, AC004089.25, AL096712.20, AC008770.6, AL008629.9, AC090043.1, AL354932.26, AC004834.2, AC011464.5, AC007956.5, AC069255.18, AP001732.1, AC005015.2, U67828.1, AC010326.6, AP001725.1, AP000553.1, AL049849.1, AL022147.3, AC011520.3, AF049895.1, AC025280.4, U95740.1, AP001630.1, AC034193.4, AL445483.13, AC073136.6, AL138787.11, AC000052.16, AC007999.12, AL353739.4, AF192304.4, AC004941.2, AC018808.4, AC068553.7, X55923.1, AC012442.7, AC018695.6, AP000567.2, AL357560.11, AC010470.6, AC004971.3, AC003101.1, AL132716.6, AC016026.13, Z97989.1, AL109823.23, AL022322.1, AC010651.7, AC004019.20, AC007537.3, AC020584.9, AL355922.4, AP002007.4, AC001497.6, AC004158.1, AC018682.4, AP000963.2, AL021393.1, AL078472.3, Z83840.7, AC007021.3, AC006433.18, AL356863.11, AC073866.16, AC008569.6, AC009244.24, AL450342.14, AC007016.5, AC015982.9, AL121787.22, U67829.1, AL118506.27, AL359853.18, Z83826.12, AC090042.1, AL161747.5,

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HAGAI85	19	381942	1 - 1738	15 - 1752	AL326844, AL534504, AL532583, AL526885, AL534503, AL532762, BF791804, BF979873, AU139874, AV706645, AW952336, BF979324, AU139805, BE615117, AW189934, AU129651, AW572808, AU158184, AU613227, AW969259, AA854118, AI057339, AW029537, AI810068, AV725299, AI460229, AU151734, AI676226, AA450163, BF217638, AI242616, R76281, AI004063, AA450100, AI095551, H46944, W03356, AI075684, W31703, T86800, AI339293, R85337, AA468695, H94753, H46945, AA323897, R77461, R77559, R26135, H43527, R80736, AA772424, H60113, R63353, H12406, H12407, R85338, R76558, R26349, R63354, AI609126, R68089, R68131, R80737, AW103602, AA745911, H59459, AI122795, Z41708, AI248729, AI800670, AW798408, BF931590, BF896996, BF735086, BE929484, BF903415, AV724914, U83461. 1.
HAGAM64	20	626997	1 - 2307	15 - 2321	BF925125, BF925123, BF925124, BF925118, BF925117, BF925120, BF925126, AA564576, BE159227, AC009466.17, AP002853.3, AP000880. 4.
HAGAN21	21	102695 6	1 - 829	15 - 843	Z69655.1, AL391987.15, AC004841. 2.
HAGBZ81	22	456414	1 - 1368	15 - 1382	AL532808, BF356940, T26989, F07451, T26988, BE089554, AV753931, AA176259, Z38391, AI652752, AU123074, AU132666, AV753734, BE876059, BF911695, AV751178, D61463, AI267311, AW387165, AW178928, AW374679, AW374832, BE089568, AW374731, BF700420, BF914304, BE173287, AW178920, AW751520, N83868, AW387129, BG170148, AW374762, AL120973, BE933886, AI915992, BE004012, AF224469.1, AF306765.1, AF184241.1, U03109.1, AF289489.1, S83325.1, AF224468. 1.
HAGDG59	23	534165	1 - 1720	15 - 1734	AV694248, BE895909, BE903848, BG027942, AV651246, BG109867, BF240140, BF217526, BF669125, BE779936, AV650099, BF971092, AW875350, AW956342, BF107182, BF697022, BG166672, BF030619, BE881774, BE548671, BF247518, AI888053, BF667451, BE872808, AI768748, BF792803, N37046, N23484, BE872350, BF239058, AW664126, BF107464, W88681, AW338066, AW952476, AW402833, BE971415, AW853145, BF968304, AI636324, N24759, BF665132, BF213364, AA830565, AV697089, AA167203, AW023148, AI815125, AI685119, H98763, BE465545.

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HAGDI35	24	597444	1 - 1343	15 - 1357		<p>BF308663, AW993425, AW954450, AI692203, AW992918, AL522858, BF110568, W72362, AL134648, AW993463, N49936, AW510670, BF528906, AW006483, AI693954, BF515443, AI887176, AA535442, AI818606, AW168954, AI863099, AW291090, AW004709, AI360443, AI871700, AW006630, BF061393, AI470191, AA594619, AI199309, AA594612, AA679412, AI076538, AI298920, AI763185, AA743895, W61171, N71964, AI683722, BF752331, AI475627, AA625964, T66225, AI631360, BF445267, N90078, N52716, W74041, AW993254, N25346, AI432537, AA826113, T48369, AI336067, BF431794, BE671301, AA774516, H15425, BF438813, AA830282, AA527245, AW150654, AW973902, AI919260, W38528, AA514881, AA928383, N99697, AW770540, F09904, AA848116, AW953438, H73840, N95112, Z39718, AA723406, W25793, F02624, AA093707, BE047849, AI350675, T97677, W61133, F02974, AI912353, AA827092, AA380688, T97676, AW270105, F12279, Z43661, F06328, AA668886, AA628658, AA830323, T48368, AW517354, N66000, BF833202, AW118678, AA351923, AA093722, AW189868, AW086208, AA767210, BE888973, BE841233, W58358, BF507840, AL522859, AW844212, N56545, H15480, AL513693, AL355334.26, AL391137.11, AL353957. 1.</p>
HAGFG51	25	823509	1 - 1299	15 - 1313		
HAGFI62	26	704425	1 - 989	15 - 1003		<p>AI693333, AA774471, H49659, AA009946, AW664812, AI217416, R56893, T88930, H44134, R67277, F10016, R52911, R39072, D61015, AI972242, Z44064, BF790840, AI090826, F06072, Z38995, R35532, AF131817.1, AF198490.1, AF181450. 3.</p>
HAGFY16	27	778820	1 - 1949	15 - 1963		<p>BE613319, AV687447, AV725712, AV687625, BG166531, BE612728, BG114876, AW952404, AV686519, AV725638, AI061630, BE877777, BF055022, BF692350, BF439548, AW372569, BE866270, BF967994, BF732575, AV706186, BG054984, BF690981, AA813278, BE876393, BF206792, AW160677, AV728247, AI612729, BF210620, AW167859, AW167862, AA521082, BF698977, BE645016, AW753532, BF195583, AA161332, BF665995, BF446480, AI887683, AA843967, BF445077, AA447934, BE348758, AA525839, BE881059, AA843171, BF673423,</p>

AA402367, AA910679, BF195330, AA037122, AW068627, AI816253, AI869290, W56256, AI806813, AI912708, AW156905, AA779099, AW206294, BG168894, N35917, AA781082, AA496466, AW022886, AA873496, AW003760, AA992894, AI168731, BF028133, AI091239, AI422091, AI802199, AA287895, AA774263, N22752, AA056053, BE042949, AA843277, BF001600, AA283859, AA287736, AI057601, AI678620, AW403982, AA984140, AA907413, AW275342, AI091181, AI361356, BE218417, BE327200, AI290167, BF572327, AW157133, AI929639, HI5827, N94537, AI685261, AA931689, W17196, BE538941, AI027113, W33009, AA293343, AI079727, N30220, AV749347, N92441, W23456, AA410485, AA935683, D58802, N27027, D81853, H99819, N94329, BE702242, AA452710, BE383297, BE218532, AI816334, BF681161, AA258458, BE077323, AA910558, AI128706, AA664059, AI446094, AW161562, BE673987, AA872758, BF762393, AA861311, N59261, BE167341, N34534, AA846407, AA918516, AI004733, AA911982, AW516664, BF762409, AA973796, AW073424, AA448868, AA857543, AA399445, AA515285, BF692523, R90917, AA399423, BF036554, AW470953, AI566161, AA725042, AA872812, T63367, AA995135, AV684142, AA643728, AI027067, AA293329, AA085090, R56184, BG109166, AA577338, H23642, AV650608, BE928331, H41386, R64440, AA029562, HI3310, W46630, AA114922, AW513259, N57112, AI423456, AA744562, AA993782, AW160789, AI245725, AW162091, AA744564, N40152, AA029728, Z43644, BF436213, AA837702, Z45519, AV689458, AA620561, AV686647, AI973249, AI093848, AA410303, AA602387, R32391, AA421573, AA258388, AA922986, BE564509, C14582, R12614, AW083148, N36220, AI499779, AA055763, AI571822, AA939289, R90813, HI6135, F06244, AW162345, W92571, N89859, AI027262, AI149386, AW023549, R63828, AA311835, H38655, AW517389, AA782100, AI348632, AW015099, T54934, AI826301, AI570545, AI207050, AI360861, W30811, AI028088, AI768693, N68929, AI307614, AA112870, AI343572, AA724357, R32390, AA807259, AI744258, AW276195, AA055962, R42373, AA613126, AI167826, R18327, BC004317.1, AC004752.1, AK025312.1, AL583915.1, AL353956.1, AL122045.1, AK025209.1, AK026480.1, AL389935.1, AK026542.1, AF058921.1, AL136790.1, AF159615.1, AL122050.1, AF125948.1, AF217982.1, AL049382.1, AF353396.1, AB063100.1, AL162002.1, AL080163.1, AJ299431.1, S78214.1, BC003695.1, AK000450.1, AF358829.1, Y16645.1, AK025414.1, AF321617.1, AL136928.1, BC002454.1, BC000556.1, AL353940.1, AK000718.1, AL137429.1, AL136844.1, AL512689.1, AL442082.1, AK027193.1, AF061573.2, AL122123.1, AK000618.1, AF217966.1, BC004958.1, S76508.1, AL137537.1, AK025375.1, AB047904.1, AL133665.1, AL137547.1, AL080159.1, BC006480.1, AK026885.1, AL117460.1, AL110158.1, AL050116.1, AL136893.1, AK025465.1, AJ012755.1, AK026550.1, AL133557.1, AL389939.1, AL049452.1, AL137533.1, AL133113.1, AF106862.1, AK027204.1, BC008365.1, BC006332.1, AK000418.1, AK026642.1, AL049314.1, AF143723.1, AK026865.1, AK025378.1, BC009033.1, AB060826.1, AB052191.1, AK026746.1, AK025541.1, AL137550.1, AF090901.1, AL110222.1, AL389982.1, AL136799.1, S61953.1, AF026816.2, AB048953.1, AL137271.1, AB055352.1, AL137711.1, AB050431.1, AF274348.1, AL096744.1, AF274347.1, AL117432.1, AF271350.1, AK026408.1, BC007326.1, AL136850.1,				
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HAHDB16	28	635412	1 - 782	15 - 796	

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HAHDR32	29	635357	1 - 1242	15 - 1256	AW767324, AW976385, AL121194, AA972628, AI095851, AA743343, BE566411, AF118928, AW366882, D20570, AC009802. 13.
HAIBO71	30	490848	1 - 738	15 - 752	AL519706, AL526798, AL525802, AL525691, AL522375, AL525839, BE792809, BE743896, BE796567, BE274399, BE260643, BE543107, BG030916, AV714392, BE889610, BE277440, BF527074, BG110983, BG181079, BF027018, BE264922, BE386448, BE382754, BE407284, BG113064, BG032444, AW991399, BE884015, BE772873, AI309611, AA442698, AW249227, BF310578, BE312050, AI421417, BF685976, BE259606, BE618656, AL522376, AW248427, BF970944, AI300569, BE564324, BE207989, BE387042, BE261799, AL531714, AI884919, AW005650, BE061923, AW960504, AW601219, BF342013, BF848073, AL525736, AA564704, AI089642, AL040087, W60773, BE207992, AA903950, AI309614, AI085644, BF347393, AL526831, AA258978, AA009753, AI419210, AA216411, AI865848, AI683537, AW117839, AI206510, AL519707, AI620366, H58361, BF752057, AW373946, BF752053, AI520851, AL525315, H42973, W42711, AW601221, AW016488, H08339, F22598, AA494395, AI005664, AI372774, H58750, AI565541, AA778118, AI828095, BE796020, AI225112, AA576831, BF347545, AA971475, AI339860, W42904, AI096947, W60487, AI243479, AI961803, AW780312, AA449981, BF760874, AA706303, AA975280, BF796645, AI126822, BE796322, W57667, AI096594, AA917878, T16862, H94211, H24045, BE718404, BE831302, H42902, R08029, F11443, F09106, R08078, BE718388, BE718374, Z43495, BF846294, BE718393, BE718373, BE831316, BE831321, AI446598, BE718398, BE718392, Z39564, BE831301, AA608866, AI245647, BE718387, BE718386, H08338, AI564884, BE718381, AA301909, BE718412, BE718462, BE718376, BE718450, T69855, BE718396, H80027, BE718385, BE718378, AA135410, BE718469, BE718384, BE718433, BE718463, BE718416, BE718439, BE718440, BE831330, AI091920, BE718406, BE718461, BE718474, BE718473, BE718391, AW247973, BE718428, BE718421, AA889882, BE718468, H24152, AI472790, BE718464, BE718414,
HAIBP89	31	727543	1 - 2229	15 - 2243	

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HAICP19	32	422672	1 - 1610	15 - 1624	AL533390, AL529681, AL528191, BF966576, AL523718, AL528190, BG120879, BF115284, AL529855, BE785817, BF026199, BF966448, BG114227, BE386416, BF115429, BF304689, BF304827, BE728367, BE793198, AV704155, AL529854, BE260405, BF305469, BE789342, BE297311, AW993505, BF316927, AW993825, BE277343, AW993830, BE265484, BF727063, AW960096, BF831956, A1743647, AW965178, C17555, BF838669, A1923650, A1860279, BF057404, AW005358, A1146421, BF928251, A1093908, BF747949, BE047374, BE813316, A1769656, AA605064, A1241016, A1148817, A1318082, W31773, AA565734, A1630731, AA843395, AW025017, A1566682, BF955698, AA506224, AA749014, AA827318, AW134754, N31961, BE774133, F36487, AA346026, T49220, AV750102, W04672, F31348, N31991, A1827206, A1630730, T49219, BF990595, A1678457, AA879426, AA120831, AA948142, AA345290, A1685001, BG007518, BG011225, AA120830, BE774243, BG004311, BE073338, BF155353, T39496, BE774391, BG007508, AW374473, AJ299442. 1.
HAIFL18	33	676933	1 - 865	15 - 879	A1670135, A1460009, A1375542, A1338350, AA362719, AA482775, AW963333, BE160727, A1282511, BF339636, AW022897, AV757341, AV731764, AW274925, BE504746, A1254779, AW408047, AW407578, AV734583, AV731604, AV731603, AU121168, AL121904.13, AP001711.1, Z85986.1, AC009267.15, AC011485.6, AL354928.9, AP000960.2, AL132768.15, AC007358.2, AC005058.1, A1049795.20, AC005245.1, AC034193.4, AC005971.5, AL034406.1, AC002310.1, AC018808.4, AC002299.1, AL354815.10, AL121897.32, AP001705.1, AC083863.2, AL158040.13, AC008770.6, AL121601.13, AL360080.21, AF053356.1, AL138725.19, AL139801.17, AC008736.6, AC010422.7, AL139009.14, AC020908.6, AF130342.1, AC006288.1, AC010494.4, AP001688.1, AF228703.1, AC005562. 1.
HAJBR69	35	638516	1 - 741	15 - 755	BE262907, AW503376, AW503644, BF982382, BE079288, AW504239, AA701415, BF315343, BE277664, BF921555, BF736464, BF756620, BE720223, BE815902, AA490675, BE930704, AW971745, AW804686, AW392670, BE695785, AW861944, AW604723, AW877209, AL119483, U46351, AW858526, AW858525, AL042984, AL119497, AL119324, AL119319, AL119355, AW500561, U46349, AL134538, AL119457, BE705903, BE705906, AW577135, AW372827, AW384394, AW861889, AW858455, AW363220, U46350, Z99396, AL119484, AL119363, AL119391,

HAIJBZ75	36	618530	1 - 2075	15 - 2089	U46347, U46341, AL119443, BF868687, AL119444, AL119341, BF868697, AW604726, AL119439, BF868684, BE705905, AL119522, AL119396, U46346, AL119335, AL134531, AL134533, AL037205, AL134920, AL134525, BE705904, AL119399, AL043029, AL119496, AL119418, AW861954, U46345, AL043011, AL042614, AL042975, AL043033, AL042544, AL042965, AL134542, AL042450, AL042542, AL043019, AL043003, AL119464, AL042551, AB028986.1, AB026436. 1.
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HAMFK58	37	647105	1 - 771	15 - 785	BG166755, BE797428, AL529398, AW439814, BE966473, AW026131, AW149540, AU148440, BF940933, AI608873, AI669338, BF331001, BF751518, AU152852, AU153427, AW771147, AW474975, AI860693, AI161399, BF031508, AI196512, AA767364, BF243271, AA573918, AW105335, BE538371, AU152980, AI860554, AI961324, AW576719, AI090203, AI421437, BF184939, AI564597, BG171613, BG252183, AA640452, AA553686, AI378739, AI951227, AA640792, AA523621, AW007941, AA159330, AA805371, AI141295, AA663960, AI078330, AA582142, AI344701, BG004337, AI891016, BF804222, BF129108, BE887740, BF344072, AI890998, AI248848, AA652054, R91906, BE906934, AW105523, W44400, AW340747, AI400158, H58083, AA146834, AW337916, BE939699, AA639362, H69285, H69284, AW088381, R52376, AW969996, AW967822, AA587731, R20938, AI751024, R78105, BF804214, BG249967, AU156032, AA772174, BE769648, AI588839, AI905475, D63059, AI783915, BG110403, BF154795, AI520663, AA062655, AW269943, AW868901, N70292, AW868763, W74046, BE906817, BF800347, BE171159, AA481220.

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HAPBS03	40	656755			

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HAPNY94	42	699770	1 - 728	15 - 742	BG029349, AW384082, AI653230, AW384103, AW590965, AI952047, AW474522, BF514114, AI952951, AI1138532, AI1199860, AW474480, AI655852, AI656352, AV727834, AI424794, AA909918, AI377297, AA632416, AA205078, BG150070, BE243783, AA709293, AW016441, AA906134, AI350684, AI825691, AW770135, AA971473, U51144, BE867482, AA770535, AA873641, BE160147, BF772564, BE184408, BC002538.1, AL133351. 33.
HAPPW30	43	135227 8	1 - 1458	15 - 1472	BF568560, BF309463, BF568858, BF968457, BE729680, BG121453, BE044480, AW958703, AW957664, AW341517, AA868588, AA479992, AA758865, AA305964, AI276502, AV696016, AA846842, BF963424, AW510684, AI183515, N41325, BF674083, AW273135, AA954695, AI685296, H57026, AA969117, AI147710, N95033, AA962530, AV650263, AA758255, BF929642, BF798962, AI337591, AA150989, AI675402, AA775255, AI167695, AI798973, AW172620, AI359078, AI688288, AI151098, BE931071, AI911606, AW469667, AA383301, H83172, AW749394, AW603134, AI188832, AI078598, H58146, AA446238, AA310796, AA724109, AA864698, AI240610, BF033606, BF854704, AA953573, AA421572, H41807, W15373, H48433, H46522, AJ739312, AW956749, BF951265, AA977855, AA757910, H87382, AI216014, AA877407, AA098821, BE168746, BE208218, W38885, H46521, R11443, R19191, H82944, C04986, AI479980, H56935, W72627, AI216655, AA975974, R99133, AA922234, AA339733, AA375160, BF352033, AW183259, AA421590, AI459843, BE930311, BE930299, T61945, AI216656, AI902298, H70309, AI902295, AI191499, T71506, AW844824, AA383302, N57057, BF800855, AA150942, AA568552, T62175, R94393.
HAPQT22	44	587601	1 - 621	15 - 635	AI002744, BF680944, AW732188, AA167511, BF868994, AI979005, AL157938.22, AP001711.1, AC013356.8, AC022217.5, AC005225.2, AC090942.1, AC011811.42, AC005052.2, AC020915.6, AC066589.3, AC027319.5, AC005098.2, AF109907.1, AC008569.6, AI135927.14, AC007227.3, AC020931.5, L44140.1, AC020558.4, AP001725.1, AC011487.5, AL034405.16, AC011465.4, AC004382.1, AC009244.24, AC004801.1, AC004526.1, AC009086.5, AL050341.18, AL139316.5.

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HAPUC89	45	834358	1 - 1139	15 - 1153	AL525296, AL522464, AL521417, AL533389, AL521416, AL524355, AL526414, AL526331, AL530863, AL524354, BE311955, BF725110, AL264358, AL669655, BF036463, BE312775, BF984883, AA477724, BF314033, AL530380, BE937625, AL526176, AL523655, AL530864, AW139040, AL520874, AL526455, AL126122, AL823620, AA312871, AL530093, AL857695, BF315809, BE256735, AW440406, AW271360, AL523656, AL200833, AL024780, AW136150, AW134590, AL522465, AA496351, BE924996, BF476679, AA292746, T55664, AL367466, AA496400, AL274000, AL283242, AL801876, AW068036, AA583620, AA477725, AA829681, BE797269, AW136110, BF822582, AL554612, AL922256, AA758054, AL533433, AW591703, BE735184, BF344330, AA296469, AL017151, AA293719, AA427485, BE562900, AW300774, AW889471, AL863281, AL424169, AL291789, BF445650, AL525339, AL670976, H01676, N55872, AW952132, BE242458, H01677, AA364430, BE735989, AA318820, AA508789, BF311298, BE397771, AA301453, BE785480, BE893629, AL248018, BF032466, BF342490, AL540614, BE264109, BE926389, BF309156, AA232553, BG255921, BE392626, BE261742, AL085402, BE206819, BE276164, BF312350, BF206486, BF763257, BG252820, AA642901, AW188803, AL758262, AA908888, BF207123, AW137361, BE258582, BE384894, AL093805, BG257985, AL751518, BF810986, BF337632, BF796886, BE397750, BE504399, F19099, AA610640, BF794720, BG104721, AL581186, BC002494.1, AC004150.8, AW003948, BE044439, AL968397, BE467670, BE326659, AW026300, AL422743, BF026131, AA921765, H74227, AA765813, BE246373, AW630293, BE671926, BE698423, BE933123, AL121985.13, AL276429.2, AF291815.1, AL271869.1.
HASAV70	46	130078 2	1 - 715	15 - 729	U69188, AW967218, AA524082, AW964322, AA477567, AW135981, BF436586, H14669, AW965610, BE870961, T62872, BF356026, AL309281, AL653643, AA629824, BF507821, AL268700, BF799497, AW607114, BF437588, AA307058, AA662791, AW204504, AA985578, AL831853, T09193, H05165, R44815, T62722, Z39918, AA477443, AA514678, BF962688, BE784445, BF184514, R41285, AW953430, T08773, T33866, BE539074, D61598, AW571983, BE702716, BE702704,
HASCG84	47	603947	1 - 1065	15 - 1079	

HATAC53	48	135227 6	1 - 1945	15 - 1959	AA345841, AL039974, BG058150, BG250744, AV728806, AA830749, AA761343, AB033058.1, AL139109.14, M85165.1, AL049426.1, BC004934.1, AL096720.1, BC000235.1, BC002816.1, BC000761.1, AK026950.1, AB056798.1, BC003637.1, AL136635.1, BC003122.1, AF098484.1, BE090917.1, AL870866, BG231683, BF677384, W72843, BE856898, AA332556, BF447208, AA772868, AL083630, AA056018, BF920128, AL130854, AA469081, AA661635, AA457490, AA130359, AL199995, AA931966, W67527, W76412, AA630878, W67545, AA458753, AL183475, AA296889, W81565, AW513265, BG023825, BF109158, AA826675, W81612, AA989066, AA076945, AA077497, AA077528, AA077040, BF515950, AW955816, AA296961, AL243042, T12258, AA056067, BE546107, AA027306, AA077342, AA026401, BE937756, AL18951, AL18971, AA022530, AA022531, BE077324, BF569541.
HATBR65	49	635514	1 - 798	15 - 812	AW754098, AV747079, AW964560, BF827304, AL697254, AA826321, AA663880, BF924786, AA772037, AV725414, AA826164, AA663006, AA826322, BE062047, AA835931, AA319870, R95053, AV760830, BF918713, BF959165, AL053538, BF930635, BE828744, AA078591, AF139781, AA491430, AA078183, AW393403, W74390, AW578861, AW393400, AA320812, BF840307, AA078213, AW752269, BF757569, AA077448, BG004304, AW793003, AA047825, AA001509, AA076683, AW857010, BE183669, BE183617, BE699552, AV720211, AW973541, BE932909, AL254770, AL284543, AL251203, AL249853, AV743864, AL251284, AW276678, AW966385, BF952670, BE707812, AL251034, AL250552, AW970571, AW869794, BE139139, AA609826, AW303098, AA552586, BF952311, AV719632, AV718487, AW905386, BE138387, AV720104, BF952747, AA015737, AW975623, BF129140, AA076784, AA604865, BG222875, AV720729, AA504818, AW905269, AV754716, AW969831, AA501867, BE042006, BF589824, W72324, BF691892, AL954192, AA610381, AA503018, AA747757, H04977, AA904211, AL912401, AL279417, BE968744, AC004084.1, AF030453.1, AC005088.2, AC004951.5, AC018720.5, AC007078.3, AC004980.4, AC007000.2, AC006480.3, AC004878.2, AC006014.2, AC007003.4, AC005488.2, AC005098.2, AC004867.5, AC004166.12, AK021477.1, AC005071.2, AC005236.4, AP000350.1, Z95115.1, AC073462.8, AC007792.1, X51956.1, Z95331.2, AC022382.3, AC087071.2, AC005291.1, AL035495.13, AL162424.20, AC002107.1, AC002106.1, Z98884.11, AF168787.1, AL157791.4, Z82215.1, AF172081.1, AC008116.8, AL008729.1, AC018809.4, AC079141.7, AC011811.42, AC006111.3, AC020358.4, AC007766.1, AL162426.20, AL139317.5, AL1390838.26, AL031005.1, AL161779.32, AC004477.1, AC008392.6, AL162615.13, AC009509.7, AC003690.1, U95740.1, AL034372.33, AF196970.1, AF253417.1, AC000062.1, AL109825.23, AC024028.10, AL034553.12, AC003030.1, AL591398.2, AC005899.1, AL034400.2, AC073492.18, AC011473.4, AC005772.1, AL139316.5, AC006487.8, AC011472.7, AP001929.4, AP000963.2, AC072061.8, Z98051.6, AC005327.1, AC007225.2, AL109804.41, AC006057.5, AP001711.1, AL136984.20, AC009506.5, AL139100.9, AC008397.7, AC007199.1, AL137162.25, AF190464.1, AC009247.12, AC025430.5, AC005261.1, AC006357.5, AC005325.1, AL121880.21, AC008395.6, AP000314.1, AL353715.21, AC025166.7, AL049779.6, AL355336.15, AC011479.6, AC011495.6, AL359644.10, AC020904.6,

HATCB92	50	603948	1 - 1742	15 - 1756	AC004706.1, Z98044.13, AL049874.3, AC007201.1, AL161757.4, AC007130.2, AL139415.10, AC02384.4, AC008738.6, Z95114.19, AC090841.1, AC005378.2, AC022001.3, AL031848.11, AC018494.6, AL445435.11, AC002128.1, AC018811.4, AC007685.2, AL121601.13, AC004805.1, AL353777.18, AL359397.3, AC0078818.19, AC007679.4, AP001781.4, AP000563.1, AP000194.1, AC007956.5, AC020633.3, AL021155.1, AC009131.6, AL359236.4, AL391839.9, AL391259.15, AL096701.14, AC008079.23, AC039056.7, AC005256.2, AL353812.13, AC004263.1, AL023553.5, AC008551.5, AC005932.1, AC079602.15, AP000133.1, AP000211.1, AJ011930.1, AL356354.10, AL163300.2, AC007066.4, AC006441.13, AC005586.2, AD000684.1, AC000134.14, AL021878.1, AC002369.1, AL032821.2, AC009510.9, AL096791.12, AC009161.12, Z82208.1, AC008641.6, AC005056.2, AL049869.6, AC023105.7, AL355312.24, AP001718.1, AL136179.15, AL078461.38, AF279660.2, AC004873.3, AC010205.5, AL353692.14, AC013726.7, AP000497.1, AC010530.7, AL133320.8, AD000864.1, Z82214.23, AL356805.5, AP000471.2, AB045360.1, AF001552.1, AL359382.23, AL450465.12, AL354815.10, AC005933.1, AL121754.18, AC018695.6, AC010618.7, AF186190.3, AE006467.1, AC002126.1, AL035681.13, AL354866.10, AC009238.4, AC007240.2, AC020946.4, AC013467.8, AC011449.6, AC004522.1, AC020945.6, AC010605.4, AL035086.12, AL049843.18, AC005231.2, AL136228.8, AL033526.24, AP002456.3, AC008080.1, AF181668.1, AC005800.1, AC011455.6, AC013355. 7.
HATCP77	51	748244	1 - 2084	15 - 2098	AI253043, AA621792, N84222, AA094505, AL522648, AC009244.24, AK025372.1, BC008349.1, AB020635. 1.
HATEE46	52	565618	1 - 1661	15 - 1675	AI791525, AI733035, BF434939, BF433029, AI457816, BF478158, AI299145, AA910198, AA952936, AI301175, BF446488, AA904191, BF477842, AF209747.1, AF099137. 1.
					BE739761, BE867642, BG252738, BF670373, AI590088, AA452296, AW188012, AI467834, BF110214, AI698059, BE535889, BE220673, AI076779, BG170578, AW304047, AI653610, AW070709, AA015580, BE300577, AA705209, AI458930, AW173124, BG149183, AI037932, BF671524, AI597851, BE671575, AI310753, AI051897, AI128681, BF447913, AW295982, BF433016, AI300950, AI140885, AW473730, BF448227, N35880, AW770729, BF108371, R72042, AW302140, AA479329, AW023183, AA040787, AI494017, H98707, AI453020, AI932397, AA041222, AI038152, AA478593, AI459059, AA151356, AI168123, AI160559, AI125997, AI702632, AI073784, H97885, AV746537, AI433746, AI348429, AI025926, AW178814, AA035147, AI917957, N26242, AI189919, AI298395, AA225891, AI383747, AW085003, BF431762, AW079138, AI214632, H57061, N27692, W20186, AI537044, AI796916, AA661665, AI290329, AI383748, T39342, H99889, AA045544, BF433765, AI948963, AI143362, BE044374, AA767678, N36000, AI203768, H88073, AA311260, N91032, AW794932, N27062, AI382971, R19439, AI037915, AA829174, N24274, N50690, AI702532, AI192385, AW166934, AI979183, AA664910, AA056938, R20449, N92329, AI625107, N43958, AW193300, AA095102, AW888582, AI160547, AA515467, N36021, N28575, N50773, BE536609, AA054589, BF694768, N73785, BE814490, AW606976, BF942077, N99407, AA151355, BF942458, AW663523, BE046513, AA897347, AI829594, BF130347, BE814323, BF089510, BE738984,

HB AFJ33	53	625916	1 - 1266	15 - 1280	AL133574.1, AL117450.1, AK027342.1, AL134941, AI936102, AA806752, AI922844, BE396072, AI568741, AW593236, AW152304, AI417415, AW629175, AI017620, AW055249, AW166099, BE858335, AA115732, AI127303, AA576745, AI829922, AI478929, AI355013, AW593259, AI814920, BE301136, BE858329, AI424011, AA975643, AI032624, AI457317, BE858317, AA733170, AI334944, AI151526, AA478034, BF195105, AI291127, AI690771, AI220431, AL043583, AA593974, BE795539, AI096520, BG251676, AI094885, AI831777, AI143003, AA204724, AW080063, AA687374, AA179553, AI373929, AA961480, AA677252, AI539748, AI150654, AI811537, AI565632, AI138450, AA931056, AA974477, AA889899, AW070496, AA886867, AI360841, NS1090, AA427863, AI499657, H99368, AI347782, BE613141, AI362268, AI369607, AA179986, BE619719, AA039351, BE350785, AI200968, AA134403, AW263162, BF939644, AI376627, AA642471, AI133209, AA035355, AA224345, AA854796, AI123495, H93126, AW821145, AA872914, AI707705, AW935023, AA804238, AI312418, D80144, AA723522, BE766774, BE834005, AI445884, BE766739, AI520801, BE177107, AA032258, N98499, T33101, BE742708, C14225, D51441, BF664500, H59455, BE082634, R96670, AW009711, BF093621, AW935098, H52680, AI265911, AI129147, BE177074, T74907, AA782664, AA568793, BE743686, D31233, BF670650, AW022342, BF336698, BE082719, R97433, AA152475, AA427988, AA365942, BF975267, AA099862, AI372406, AA922699, T33142, T32913, F34614, AI676138, N34899, BF879062, AA852622, D80145, AW794944, AI352444, AA363998, T30009, AI372746, BF873002, H08716, W31065, BF872967, W28879, AW881570, BE547161, AA312863, AI039527, AW082087, BE771401, R70284, BE262112, BF340241, AA319768, AI420273, AA88050, AW513743, AI583354, BF349629, C14224, AW881571, Z38385, AA443158, AA354867, AW881573, AU149417, AI914657, AI277700, BG231859, AA910603, AI961888, BE717468, N54216, AV727127, AI911845, R91976, H56262, BF975357, AA661955, F04560, AW364002, R41447, BG255586, T75007, AI857675, AI076059, AA627769, BE717493, AW754481, BF690414, AW799938, AI797975, AA478191, AA548786, W22044, BE939215, BE081547, BF378280, BF365011, T24992, AW381095, AW839942, AW363800, AI124578, BG166902, BF770472, C01685, BC000778.1, AK025162.1, BC008847.1, AF214731.1, AL136886.1, Z48570.1.
HB AFV19	54	843036	1 - 939	15 - 953	AL516557, AW273167, AW301700, BF795352, AA704856, AI808501, AI633808, AI050770, AI500656, AW902226, AW964585, AA480361, AW445068, BF354764, AA886018, AA886008, BE535750, BF307524, AI480277, BF960307, AA321228, AI565943, AI493176, BF960304, BF336986, AW027985, BF308034, BE159877, AI653941, BE829951, AW664513, AI135012, AW858522, AW577199, BF084778, AW601637, AL134110, AL045494, AL134524, AL042523, AL045327, AW577201, AL042420, AL042468, AW577192, AL045328, AL047163, U46344, AL042741, AL042655, AL042898, AL136927.1, AK025498.1, BC009255.1, AF001781.4, AC000381.1, AL136764.1, AL136762.1, AL133053.1, AL136763.1, AL136755.1.
HB AMB34	55	553553	1 - 1013	15 - 1027	BE673228, AA771964, N93148, AA844453, AA782604, AA936090, AA594712, Z23123, AW015698, AI589136, F00234, AA479120, AI301192, BE348256, AI769699, AI870557, AA676477, AW074427.

						AI216517, AI378183, AA505080, N34510, BE644673, AA854947, AI355342, AI915783, N51070, N39571, AI568614, N57476, BG107565, BE670027, N47320, BF437948, AW071941, N66687, AL353708.10, AL031591.19, AC022407.6, AL354809.12, AC007350.1, AC005921.3, AL445928.8, AC005068.2, AC002542.1, Z75747.1, AC006252. 4.
HBCPB32	56	135240 3	1 - 1354	15 - 1368		AL522529, AA776274, BE439690, BE439637, AI421729, AI421796, AI031855, AI418669, AL522530, BF312464, AL530028.
HBCQL32	57	113495 4	1 - 388	15 - 402		AW574632, AA779803, AI420937, AI139252, AA993944, BF591447, AI631896, BE906760, AA614327, AI086516, AI017902, AI651172, BF437264, AI972275, AI023361, AI692172, AI753360, AA813167, AI381013, AW015745, AA458613, AW404165, AI351368, AA057753, AA405488, AA569272, AA383066, AW602265, BF342355, F37908, AA368651, BF840063, BF081585, AW959191, BF835219, BE717190, N51554, AW301825, AW272082, C01302, AW264472, AI659074, BC008044.1, AK024535. 1.
HBGNU56	58	135241 2	1 - 850	15 - 864		AW954217, BE875979, BG025158, BF529722, BE395207, BE734057, BE789549, BE873075, BE785505, BE614806, BE738333, BE614883, BE253565, BF340317, BF737302, AA044211, BF792671, AW796084, AW238972, BF738993, BG012029, BF812968, BE876237, AW406916, BF901660, AI342703, AA075901, H25630, BE810793, BE183450, H43485, AA296837, R95168, BF809994, BF868942, AL532494, W95348, H80718, BF804848, AA287470, AA806231, AL532493, AA298795, BF997411, AA296696, AA296826, BF082160, AA218811, AA296869, BF331433, BF829581, AA034079, AV743953, AW802996, H73675, R55519, BE140100, BF056207, AI819836, BE737872, BF446055, AA465105, BE396147, AA044081, AA583464, AI582284, AA983595, BE775061, C00212, BF771777, BF799156, BF895320, BF931829, AI537196, BF771828, AA523623, R39644, AI521467, AI952620, BE828356, AA187096, H42497, AA297863, BF763569, AW338141, BF736987, BF248485, AI346295, AI424071, AW512207, BF905334, AI066489, AI028038, AA699982, N86960, AI358167, T10507, AI683820, BF245896, BE904822, BF978464, BF811185, AA622655, BF814100, AA304509, AA595646, AA912088, AA287334, AA643965, BF747982, W95391, BE043918, BF807379, AI279829, AA722634, AI817892, AA187305, H80719, AA485829, R55520, BE671577, BF750444, AI637718, BF674579, AA873526, AW103333, AI650465, AA531049, AA658172, BG057590, AA583458, AV743642, AV739884, AV742260, AV743114, AV738121, AV736224, AV744272, AV741543, AV738375, AV738262, AV743004, AV739415, AV736083, AV737550, AV737002, AV741197, AV737715, AV742899, AV741000, AL037348, AV737101, AV739156, AV739895, AV701296, AV743288, AV740805, AV740787, AV737726, AV737727, AV744332, AV739871, AV740443, AV742357, AV743197, AC002390.1, AF177940.1, AL080096. 1.
HBHAD12	59	420036	1 - 772	15 - 786		AW905621, BE087451.
HBHMA23	60	848016	1 - 1161	15 - 1175		BF672220, AW384404, AI924632, AW167650, BF743981, AW449208, AW363590, BE693858, BF827339, BF826403, AI909935, AW167610, BE073612, BE061388, BF089104, BF088537, BE829540, AW577643, BF356926, BF827064, BF355973, BE926857, BE720600, BE934196, BF804024, BF831089, BE933114, BF742671, BF355970, AI024451, AW381927, D45555, BE934074,

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HBIMB51	61	963208	1 - 523	15 - 537		AW293249.
HBINS58	62	135238	1 - 829	15 - 843		AI827239, AW104045, AL536345, AL096774. 9.
HBJFU48	63	460392	1 - 835	15 - 849		BF674706, AA657543, AV757289, BE139139, AI250552, AI251284, AI251203, AI284543, AI251034, AW674277, AI254770, AW303098, AA582073, AI249853, AC005696.1, AF045555.1, AC090514.1, AF243527.1, AP001725.1, U91318.1, AL121897.32, AP003357.2, AC008155.9, AC005081.3, AL132838.4, AC011470.5, AP000692.1, AL132640.4, AL109976.23, AL121992.24, AL135928.6, AL033529.25, AL353807.18, AC020916.7, AL138849.12, AC011247.10, AL158830.17, AP000501.1, AL008637.1, AC006270.1, AC011464.5, U95742.1, AC022384.4, AC011555.5, AL049795.20, AL033383.26, AC005921.3, AC012170.6, AC004922.2, AC007934.7, AC018828.3, AL121653.2, Z82215.1, AC022383.3, AL049636.22, AC007216.2, AC005971.5, AC005058.1, AC010431.7, AL135783.6, AC044797.5, AP000355.1, AL121928.13, AE006462.1, AL590682.9, AL451083.5, AL162724.16, AC004906.3, AC006312.8, AL359272.9, AP001666.1, AP001716.1, AF111169. 2.
HBJIY92	64	778065	1 - 2420	15 - 2434		BF507343, AI830176, BE777697, AL134817, BE466375, BE536137, BG033415, BE770976, BF665352, AI141799, AI333231, AW083069, BF674917, AI819484, AW291130, AI693686, AI139569, AI765217, C05997, AI191712, AI360840, AW403076, AA830242, N23996, AI707975, AI360845, AV746530, AI743353, BE675302, N28536, AA737061, AW405631, AI864662, AI627462, W31857, AI492266, AW589350, AI581705, AI624651, N34736, AI860242, AA181897, AI811985, AV682516, AA812089, AA768170, BF589611, AI942262, BF572713, H99855, AI536025, AA612923, N67098, AA705383, AA082077, AA761491, AA884032, AA442783, AW977117, H00904, AW770178, AI796455, BF571118, H00903, AI568136, AA682798, BF343253, AI926340, AW591358, T91642, BE887851, BE693611, N28620, D63124, AI432722, T91587, AI740627, AL513907, AL513597, AL514791, AI433157, AL514063, AL513977, AL515413, AL513553, AL513693, BG179993, AL514627, AW087445, AI613017, AI580190, AI469532, AI702433, AL513631, AI539153, AL514691, AL045500, AL513999, BE018334, AI934035, BG260037, AL514919, AI538716, AL515191, AI564719, AI572787, BF724198, BG252914, AL514303, AV758822, AV758592, AI636719, AI687362, AI812080, AL515019, BG180996, AL036146, AL036361, AI583316, BG110797, AW169653, BF868489, AL513713, AI499393, AV756393, BE048131, BE966479, BG257535, AI524671, AW274192, AI815855, BG031815, AI446606, AI273142, BE620084, AA470491, AL514015, AW162071, AV758806, BG164371, AL514473, AL513643, BG109221, BF885675, AI687728, AI560099, AI536685, AL513911, AW301409, BG168696, BE964683, AI818683, AL514867, BE964006, BG109125, AV733397, BE967261, BF337043, AV756619, BG250190, AI781779, AV705644, AI653541, AI269696, AL514087, AI537244, BE966388, BF882343, AA640779, BF970162, AV682249,

AL513951, BE964812, BE789764, AL119791, AV756026, BF792099, AI475455, AI702406, BF342070, BE965481, AW827203, AL514025, AL036802, AW827249, AV709517, AW238730, BF970731, AL121270, AS08692, AV756150, AI349933, AV755613, BE781369, AI570384, AI436456, AW188539, AV757018, AL135661, AI868831, AW075413, BG151247, BF724691, AI499131, AI554245, AI857296, AW002342, AI224992, AI573032, AW999049, BF817926, BE018711, BF792469, BG253026, AL514935, AI633419, AI498579, AI866602, AI349004, AI475451, AI433976, AI280747, AL036274, BE964495, BF795712, AL513803, BG036846, BE963035, AI610645, AI567351, AW268220, AI439087, AI439762, AV729890, AI521012, AI872711, AI934036, AV711924, AV706164, BF792767, AI492540, AI469811, BF971016, AI539771, AV757737, BF970658, BE965190, AI866608, BE964700, BE964633, AB014540.1, AL110154.1, AF134894.1, AK027131.1, AK025084.1, AB056420.1, AF090903.1, BC001967.1, AL049452.1, AB019565.1, AF090934.1, AL117460.1, AF090900.1, AL133640.1, AL050149.1, BC008387.1, AB063070.1, AL133016.1, AL162083.1, AL359596.1, AF090896.1, AF146568.1, AL512733.1, AL136787.1, AK027868.1, BC008488.1, S78214.1, AB055303.1, AK026045.1, AL442072.1, AF090901.1, AL136892.1, BC008417.1, BC007021.1, AB055366.1, AL133557.1, AF104032.1, AF219137.1, AL442082.1, U42766.1, AK026855.1, BC008365.1, AL117457.1, AL359618.1, AL049938.1, AB049758.1, BC003687.1, AF090943.1, AL049314.1, AL136789.1, AJ242859.1, AF106862.1, AL137459.1, AF125949.1, AL136586.1, AB056768.1, BC003683.1, AL389978.1, AL110196.1, AL136749.1, AL080060.1, AB048953.1, AF218014.1, AK000212.1, AF111847.1, AF078844.1, AL122093.1, AL133080.1, AB063008.1, AB047615.1, AL050116.1, AL050108.1, AL050393.1, AB055361.1, AF091084.1, AL162006.1, AL110221.1, AL096744.1, AL050146.1, AL157431.1, AB052191.1, AL133606.1, BC006807.1, AB063046.1, AL136799.1, AL137527.1, AL122050.1, AK026741.1, AB047801.1, AK027096.1, AF097996.1, AK025339.1, AK026647.1, AL390167.1, AB060887.1, AK026452.1, AK026865.1, AK026608.1, AK025958.1, AL359601.1, AK000323.1, AB048964.1, AL133075.1, AL080124.1, AL050277.1, AL512718.1, AL080137.1, Y16645.1, AK024538.1, AL049466.1, AL137283.1, AL512719.1, AB060916.1, BC001045.1, AK000618.1, BC004556.1, AL122121.1, AK026533.1, AL133093.1, AL512746.1, AK000083.1, AL050024.1, AK026744.1, AL389982.1, AL117583.1, AL136768.1, AK025772.1, AK026784.1, X82434.1, BC002733.1, AB060863.1, AK025414.1, AB060908.1, AL133565.1, BC006195.1, AB055368.1, AK026086.1, AL137557.1, AB060912.1, AK000445.1, AK000432.1, AL049430.1, AF177336.1, AL136844.1, AK025092.1, AL133560.1, AL359941.1, AK027116.1, AK026642.1, AK026542.1, AB060825.1, AK026504.1, AL512689.1, AL122123.1, AK027113.1, AB060826.1, BC008485.1, AB052200.1, AK025484.1, AL117394.1, AF207829.1, AB048954.1, AB062938.1, AL117585.1, AF125948.1, AB051158.1, AK000137.1, AL512754.1, BC008382.1, AK026534.1, AL137550.1, AF225424.1, BC004951.1, AK025491.1, AK026927.1, AB055315.1, AL136928.1, AK026532.1, AK026592.1, AL110225.1, BC008899.1, AB060852.1, AL353940.1, BC006412.1, AK026959.1, BC002839.1, AL049382.1, U91329.1, AK026583.1, AL122098.1, AK000652.1, AB055374.1, AB056809.1, AL512765.1,				
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HBJLC01	65	638410	1 - 858	15 - 872	
HBJLF01	66	732111	1 - 1918	15 - 1932	BG261130, BG121213, BF347966, BF796462, BE899286, R17115, AL123525, AL697325, BE783654, AW402585, AA032035, BF724098, AA031919, AW402594, AW402872, AW026287, W89010, AI926967, W95778, BF887406, AI376419, BF381332, BF507805, BF888120, AA233002, AI669291, AI963299, BF744292, BF907549, BF907541, AA954836, BF888127, AI768850, AA768759, BF888128, AA232951, BF744299, AW090314, AL571824, BF888074, N73038, AA480645, N53675, AA886377, BF888119, AA535561, AI864506, BF799491, AI217778, N51612, BF381336, N53906, BE819619, AI806785, BF744934, W95735, BG251027, BF381311, AL674508, AA016130, AA743705, AA917873, AA649797, BF887394, AA631017, BF907590, AI480218, AW302053, BE139664, Z39059, H86222, AA954334, AA456896, AI244571, AA015836, AI341715, AA485019, AI078627, AI015866, AA827439, BF745018, AW271993, AA954612, AW001670, AK000208.1, AC011005.7, AC083866.2, AA830583, AA465482, AA731000, AA815064, AI632903, AW576518, AA847860, W84413, AA210914, AW341113, AA721650, AA488009, R45299, AW873717, AI693003, AW977787, AI283768, AI127928, AI148391, BE048487, AA417947, AA236463, AI671420, AA836581, Z38691, AA811097, AW471001, AA210913, AI500017, AA709242, AA418189, AI492414, AA234646, AW956166, AV703593, AW950675, AW963117, AV706278, AV701983, AW954129, AW965551, AC013414.7, AK026400.1.
HBJLH40	67	828130	1 - 1839	15 - 1853	
HBJNC59	68	112580 2	1 - 1047	15 - 1061	AW007501, AA902287, AI858092, AI005351, AW959933, BF342564, AW083940, BF820646, AI870864, AW960414, AI032697, AW149115, AA829811, AA709070, AW264612, AA643392, AI951841, AA614344, AI312642, AA533443, BF850030, AI799536, AA991955, BG222284, AI830766, AA594172, AI289881, AI741805, AI276207, AW088660, AW268666, AI749660, AI369678, AI264768,

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HBNAW17	70	526797	1 - 587	15 - 601	AA713518, AA807610, AW104604, AA830415, AW975518, AL138824.19.
HBOEG11	71	130075 2	1 - 1342	15 - 1356	BF056642, BF516162, AI807970, AI081658, AA861514, AI494148, AW448950, AI973060, AI400318, BF849398, AA385680, AW028539, BF847907, AA377456, F34025, AI472684, C01967, BF344191, BG251209, BF337896, AW079432, AI783808, AA649296, AI343030, AI334889, AW023871, BF107008, AI336565, BF911517, AW243767, BF874010, AW410046, AW151283, AL041230, BF911521, AV744830, AA836558, AL048644, AA769697, AI799189, BE892572, AW952403, AI933926, AW074057, AW020619, AA768214, BF154738, AF083500.1, AF100780.1, AF074604.1, AL139352.16, AF100781.1, BC002631.1, AK024855.1, AK024533.1, AB060883.1, AP001605.1, AP001699.1, BC001795.1, BC008895.1, AL136789.1, AL137461.1, BC008488.1, BC003105.1, BC005805.1, AB060828.1, BC005084.1, AC008897.7, AF125948.1, AL162085.1, Z49258.1, AL445220.5, AL049276.1, AK024570.1, X76228.1, BC002948.1, BC007371.1, AL096728.1, AL117590.1, AL080124.1, BC000199.1, AL109672.1, AF090900.1, BC005890.1, BC000895.1,

HBOEG69	72	793786	I - 1397	I5 - 1411	BC002535.1, AL136893.1, AL512751.1, BC007417.1, BC002816.1, BC001328.1, BC002372.1, AB048995.1, BC008751.1, AW576190, AA524064, BF701378, AI337569, AW058654, AW964434, BE568412, AW978965, AW241842, BE221243, AI346249, AW241843, AA825846, AA936562, AI184881, AI346396, AA570030, AW368546, AA465472, AW995507, AW361365, AV743550, W74158, AV750714, H80936, BF879997, BF880246, AI144077, AV743963, AV740879, AI053597, AI222773, R95913, BF901243, AA318779, BF088361, D62291, R27740, BF767423, AI277044, AV743740, AI053934, AI310256, R27741, R08998, C00592, N64904, AA827757, AK024978.1, AC006146.2, AF147723.1, AU124786, AL523480, AU125638, AA608680, BF185800, AL135214, AI346426, AW369825, AV715627, BE044175, AA704114, AU148578, AI953494, AA102088, AA099340, AA875957, AA411819, AW103703, AI339566, AI610736, W27706, AA825903, AI934820, AU149251, AI080375, AU160262, R67711, N40031, AW901194, AA315231, N27293, AA401638, AI307801, AW589999, Z42700, AA382141, Z38860, AI382965, AA774224, BF816363, R62663, R43562, AI244553, AW118387, R62613, R22885, T35989, R66107, AI204282, F10296, BF946792, BF944261, AA095193, AA093900, AI964066, AW576941, AW025279, BE048061, BG114528, AV759054, AV761957, BG105500, AI625444, AI679506, AB020705.1, AK022701.1, AK025648.1, AC005207.1, BC002697.1, AK026649.1, X99717.1, BC008365.1, AF260566.1, AL359932.1, AL137267.1, AB049849.1, AB047623.1, AJ401156.1, BC007347.1, AK027142.1, AY007109.1, AF285836.1, BC006287.1, AL049276.1, BC007034.1, BC009311.1, AF151109.1, U72621.3, AL390154.1, AF103804.1, BC003684.1, AL137479.1, AB062750.1, AK025391.1, AF093119.1, AK026642.1, AK000391.1, AW470141, AL540555, AI150724, AU120416, AA547979, AI187148, AA287570, N32944, AA255853, AI802087, AW276458, BG009661, AI923052, AW976784, AA904211, BF805088, AI278972, AW269504, BF942976, BF939548, BF725844, BF944736, AV720367, BF920612, AA812058, AA410788, AA535216, AW069227, BG056362, AW965008, BE265787, AA425924, AA873573, AV719902, AW819125, AI634187, BF804385, AI445582, AA487475, BF965394, AI160786, AA742815, AI133514, AJ608699, BF767878, AW023111, AI625604, BE139139, AI491765, AI457313, AU147162, AW505253, F28204, BF857849, AI284543, AI889579, AI251034, AL527073, AI251284, AI251203, AA470512, AA315361, AW972919, AI679002, AV760019, AA568204, AI538236, BE645220, AA847508, AV695478, AI291439, AI884383, AI047467, BF968874, AI537995, AI130709, AA730305, N59569, AW968564, AI890324, AW674631, BF725761, AI223626, AW341978, BE138509, BG250286, AI679759, AI814682, AA847427, AV725627, AI889696, AI254770, AA456924, AA714110, AW805539, AI053688, AW575000, AW131417, AA832145, AI573198, BG230549, BE138594, AL041375, AC009511.16, AC005071.2, AC020913.6, AC005081.3, AC004166.12, AC079602.15, AC087071.2, AC005015.2, AC002472.6, AL138724.12, AC005098.2, AC005011.2, AC019206.4, AC009412.6, AC007664.12, AC018642.6, AC011461.4, AF053356.1, AC006064.9, AC004841.2, AC020908.6, AC011497.6, AC005562.1, AC005102.1, AC009079.4,
HBXFL29	73	842802	I - 2215	I5 - 2229	
HCACU58	74	625923	I - 1540	I5 - 1554	

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HCACV51	75	130670 6	1 - 2069	15 - 2083	AL521141, AL521142, AL524128, AV695196, AV694072, BF338443, BG114245, AV689975, BF670146, AI760812, AV723814, BF574966, AI633691, AI907541, BF528015, AI743976, AW006271, BE549523, AI700393, AA115333, BF448307, AI768614, AI378849, AI131998, AI131832, N66024, AA151271, AI129857, AV704651, AI091145, AW380450, AI269749, AI172168, AV724434, R54280,

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HCEMP62	81	684780	1 - 1846	15 - 1860	AL520667, BF689505, AW953641, BG168504, BF343502, BE747867, BE737374, BE734304, BE514593, BE378257, BG179655, BF982990, BE909615, BG058649, BG115902, BG029850, AI688113, BE870978, AI554392, BF689070, BF690427, BE546131, AA911109, AW173438, AW382483, AA486370, AA778384, AI382028, AA776265, AW580475, BF874009, AA563686, AI493765, AI523553, AA484857, AI362311, AA811238, AA906681, BE047437, AA838288, AA460659, AI276177, AW404956, AW752131, BE763979, AA479791, BG029140, AA259052, AI097482, AW580486, AI082243, AA488079, AW510339, AA088205, AI609703, AI093069, AV683434, AW438882, AW366250, AA477188, BE141358, AI350871, AI953839, AI033274, AA285058, AA648139, AI087234, BE141360, AA226399, AA594766, BG006416, H03363, H53631,

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HCENK38	82	658737	1 - 1495	15 - 1509	<p>BG178033, BE896063, AV722833, BE907276, BE277857, BF952019, AA521308, AW182868, AA908959, AI628880, AW173363, AW665845, BE870003, AW631238, AI151418, BF996707, AI818267, BG180581, AI653663, AA001203, BE150445, R78710, AA130178, W03542, AA746655, AI828924, AA001202, AI961323, BE277870, AI093113, AI377976, AI951984, AI635625, AI624029, AI418242, AW088095, AI346936, W92652, AA130170, AA024605, W60401, N53543, AI207798, AA969140, AV706224, AA206833, AA862855, AA883077, AW173095, AW467519, BF830518, AI890288, AW952261, AA676671, R76291, AA641764, W60310, AI536758, AA742467, W92685, BF830522, C01747, BF029590, AW273508, W72474, AL047508, AI863984, W46673, AA928559, H97873, W46482, AA969604, T17266, W92828, W94587, BF963436, AA024606, AA973624, R61420, BF107415, AI932612, W76228, N72501, BE147741, AA160170, AL247642, AI499771, AW582120, N92375, AI803849, C04881, AW192182, N67695, R76925, AV728500, BF906742, AA641806, AW601191, BG104607, H00789, T31087, R61378, BE706416, AL047509, R78711, R76567, AA564390, AA992073, C15162, AI187944, AW779277, H39236, AA812071, W61163, H85007, AA733042, W61229, AI016971, H81599, H97053, R78466, H86612, H85630, AV713546, H90060, H86032, R78534, AW952259, AW889353, AA021401, AI540906, W24617, R62435, AA714924, R84855, H00689, H81598, AA918680, BE903841, T08911, BF834059, AA501896, BG106391, R40305, H86526, H85633, AA021275, R21120, H85004, AA774992, AI834279, AW970014, BE140906, N56017, AA573996, AI300746, R13223, Z43839, AI834298, AA094627, R85725, AA600097.</p>

HCEWE17	83	941941	1 - 953	15 - 967	<p>AI475228, AI834286, AW380821, H85894, AA573651, BE843503, T32504, AA010588, AW380818, BE881856, AI879932, AA92769, D55263, AA829059, AW770059, AI310325, AI022447, AA693896, R83833, BF819760, AI925934, AF193807.1, AY013268.1, AY013267.1.</p>
HCEWE20	84	543370	1 - 871	15 - 885	<p>T51653, AW168798, BG059728, AW151307, AA189081, AI133942, AI924175, AI610776, AI034217, AI479035, BE165748, AI811494, AW090210, AA346162, AW167452, AI687804, AI749571, AA470572, AW089655, AI197934, AI827133, AU144339, N64574, AA470493, AI697247, AI937684, N76274, AI984510, AL047920, AA223830, AA493998, BE176566, AV730063, T62931, BE148908, AA876415, AI801377, AW589501, AA085707, AW177317, AI439860, AI813517, AA581340, AI858607, AA099491, AA613244, AI887321, AA643785, AA633390, AU143906, AV719347, AI362951, W58428, AU146966, AA847621, AI564253, AI921101, AL041417, AA643823, AI567544, AI733077, AW177120, AI561208, AI264673, BE158597, AU145674, AA130536, AA694579, N74502, N54295, AW440317, AF063514, AU119100, AA873103, AW177237, AA160519, AA197059, AW177231, AW177264, AA598786, W49501, AA911409, N26540, BE264670, AL036881, AU146974, AA493751, AW994225, C17730, AA724159, AU145383, AA157033, AA041332, AA166854, H96719, AA055654, H65500, AA219480, AU148220, AI935333, AL523955, AI132962, AW084901, N48690, AI862874, D29455, AA598990, BE044603, AF074627, AV730577, BG235936, AA878800, R94112, AW275729, AI376984, AI951835, AA101456, AA503213, AW440351, AI735074, AW177266, BE904846, AA846188, AW177226, BE152426, AA493735, AA593081, AW615437, AI538654, AA404968, AW813744, AA669580, F03370, AA350922, AA356989, AI421079, AV728282, AW771706, N76124, AI189033, AA584498, AI961771, AA953572, AV719696, AA467957, H04879, BE159220, T69889, AV720543, H97020, AA467904, AW074001, AF282320.1, AC073310.7, AK026100.1, AL030995.1, AL445236.22, AC023160.31, AK027219.1, AC003977.1, AC008945.6, AJ271735.1, AC012172.6, AL161415.2, AL139125.18, AC002217.1, AC023892.35, AL512629.7, AC069228.26, AC011998.8, AP000075.1, AC008651.7, AL133238.3, AL359816.16, AL121694.4, AP000639.4, AC004029.1, AL121757.7, AC002349.1, AC027304.3, AC004397.1, AF003627.2, AC018637.3, AL355615.12, AB038653.1, AC011755.7, AC022468.5, AL133325.20, AL356113.8, AL121986.12, AC004636.1, AL356213.10, AL390023.8, AC008496.5, AC009812.17, AL136374.4, AC007388.3, AC005280.3, AL133404.8, AC012309.7, X14975.1, AL133240.3, AL158069.16, AC011310.3, AL356782.14, AL158055.12, AC010285.4, Z84482.1, AL359950.4, AL034428.4, AC010145.9, AL441887.9, AC003085.1, Z83836.2, AC025420.26, D86996.1, AC007392.3, AC007207.22, AC020717.3, AC022316.18, AP002532.1, AC012323.7, AC026413.5, AL590792.1, AL031387.4, AC022083.6, AL512885.4, AK021525.1, AC005614.1, AC008162.3, AL136170.12, AF248484.1, AL033524.11, AC079175.24, AC007051.3, AF127577.2, AC016396.5, AL132715.3, AL359398.2, AP000626.5, AC073095.3, AL353580.7, AL354758.14, AJ251973.1, AL034545.1, AC004551.1, AC068812.13, AP001669.1, AL590404.5, AC010276.6, Z73497.1, AC013355.7, AL031775.1, AL049570.11, AL590387.7, AC008518.3, AC003670.1, AL160236.4, Z95114.19,</p>

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HCFU88	85	553587	1 - 839	15 - 853	N21179.
HCFMV71	86	526599	1 - 386	15 - 400	AI916386, AI392712, BG035021, AL135901. 23.
HCFNN01	87	430297	1 - 1247	15 - 1261	BF592932, AI660093, AI917105, BE502245, AI435489, AI168436, BF131228, R69799, R67877, R81389, AW170015, R34017, D51015, AI283968, R69800, F08994, F08984, T16467, R81390, R67878, R33479, AI581033, BF981109, AL110306, AI929108, AI538885, AL046944, AI889189, AW858243, AL039390, BF795712, BG257535, BE963035, BG110517, BG029667, AI433157, BG252929, AI539771, AW162194, AI345688, AI537677, BF811804, AI500659, AI815232, AI801325, AI500523, BF812438, AI500714, AI433976, BE885490, AI923989, AI284517, AI500706, AI445237, AI491776, AW151138, AI521560, AI500662, AI284509, AI866573, AI633493, AA470491, AI434256, AI888661, AI284513, AI888118, AL045626, BF911521, AI671642, AL036403, AW022808, AL041150, AL513577, AI620284, AI582932, AI888665, BF812963, AI828574, AW022682, AW023338, AW673679, AI274759, AI554821, BG260144, AI648567, AW151136, BE877142, BE047852, BE897632, AL048656, BF338002, AI494201, AI889168, AI866465, AI355008, AI538850, AI623736, AI872423, AL046926, AI440252, AV729760, AI582926, AL045500, AI539800, AW172723, AI440263, AI866469, AL513991, BE886728, AI434242, AI805769, AL513597, BG120706, AI859991, AI436429, AI889147, AI355779, AI371228, AI590043, AI491710, AL047422, AI866786, AI860003, AI610557

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HCOOS80	96	113497 4	1 - 1240	15 - 1254

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HCUCK44	98	720291	1 - 1125	15 - 1139	AL532468, BE621866, AL521895, BE621760, BE538472, AL521894, AV734260, AV723629, BE770935, BE790853, AI140351, BE621673, BG168718, BF793790, BE908998, BE545559, BE616433, BE395052, BE621070, BF664130, BE937841, AI859347, AV696398, BG164550, AW977552, BE731169, BE514231, BE312999, BE717043, AV696286, BF726404, BE018100, BE717057, AA121548, AA768342, BF326554, BF430984, AI864674, AA530873, BF338307, BE717061, BE676694, AA127712, AA722381, AI815642, BE281457, BE717055, BF971805, BE795728, AA987515, BE717048, AW275917, AI354682, AI859814, BF686844, BG035461, BF977210, AW474962, AI025466, N92869, AA768339, BE396293, BE301588, AI051671, AW753719, BE965688, AI920875, BE812296, AW089493, BE535563, AW190165, AA417302, AA130959, AA587755, BE717112, AA045598, N21328, AV712375, AA314322, AA844332, AI371694, AW578738, AA100477, AA043186, AI567303, BE717183, R83064, BE891492, BF809525, AI350331, AI039892, AW193146, AA828283, AI952434, BE717068, AI289086, AW377665, AI014387, AA917482, BE560356, AA975893, N21020, AV758595, AV760858, AA621534, H94056, BE218977, BE741064, AA100476, AW406948, AI564973, AA729835, BF594159, AA417265, AI187288, AA045597, AA306867, BE548903, AA661773, BF027132, W04309, H80956, AW615725, AW088039, AI419448, AI952495, N47889, AI083853, AA649285, AI816957, BE927438, BF029994, AA580315, AW103201, R89903, AI289415, N27984, T40562, BF593347, N80197, AA868207, AI018462, D82429, AI873582, AI955989, H81296, BE616655, AW138496, AI833059, AI288157, T91268, R63140, BE044820, BF594190, AA130829, D12288, AI699667, AW952882, AI942324, AA310276, W22908.

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HCUEO60	99	499242	1 - 1208	15 - 1222	<p>AV748967, AV762395, AV761362, AV762397, BG104686, AV760057, BF668217, BF677892, AL046409, AV763971, AL284640, AV761489, AI334443, AI963720, AV728425, BG249643, AV763449, AW303196, AW301350, AV735370, AV725423, AV762111, AW274349, BF541120, AV762098, BF241967, AV763255, AV759274, AV761786, AI270117, AV740801, AV763540, BF337291, AV763670, AV762064, AL138265, BF697673, AW833862, AW023672, AV761843, AI305766, BG167139, AI431303, AW419262, AI133164, AW268973, AW088846, AW193265, AV762505, AI696962, BF131362, BF684828, AW472872, AL138455, BE562953, AW963497, AW965008, AA490183, AI281881, AA581903, AA521323, BF827410, AI610920, AV762092, BF311000, AV760937, AV732891, AV763354, AL042853, AV762535, AW979060, AV759505, AW327868, AL119691, AV762826, AW975987, AI754658, AL038785, AI345654, AW501386, AV762645, AV652936, AV763558, AI613280, AV760777, AV733830, AI064864, BE049139, AV761941, BF680074, AV764307, BF965007, AV702857, AW662543, AV734666, AA491814, AV729809, AI345681, AI679782, AL046205, AW500125, AV759352, AW265393, AV757425, AF330238, BF725504, AV699574, AV764228, H71429, AW974109, AV764235, BG109996, BF915247, AW503666, AW502975, AV759204, AA491284, AV761106, AW518220, AW972871, AA521399, AV725431, AI307608, BE276880, AV759507, AA610491, AV764578, AI345675, AW975049, AW973397, AV762009, AV761884, BF991286, AV735495, AI570261, AL041690, AA680243, AV762959, AI144101, AV760486, AL045053, AA587604, AI368745, BF679304, AV710066, AV760466, BF793766, AV761745, AW969629, AA526787, AV763633, AF074677, AI732865, AI350211, AI890348, AW953071, BE150580, AW576391, AW513362, AL037683, AA469451, AU147104, AI708009, AW410400, F36273, BG222267, AV762067, BG036665, AW872676, BE160727, AV719316, AW270270, AW029038, AI732120, AA488271, AW021583, AV763847, AV742057, AV759172, BF691714, AV713243, AA877817, AW088202, AV729947, AV759214, AW960468, AA682912, AV762139, AW072923, AV759580, AV764530, AI345518, AV760106, AI355206, AI625244, AV760736, AV763122, AW872575, AA468022, AW769399,</p>

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HCUHK65	100	651313	1 - 353	15 - 367	AI161343, ALS20380, BG111970, W84487, AA868067, AA931374, AI271350, AI080159, AA970366, AI221950, Z39489, F02802, AA213383, AI205879, N92722, T08346, R42398, AI743040, R37459, C02421, F04701, N92721, AI861833, W84564, BF062378, BG032378, AI190488, AL442092.1, AC004142.1, AB060967. 1.
HCUIM65	101	550208	1 - 861	15 - 875	BE781101, BE540200, AI972511, BE300952, AA464837, BG150212, AI681901, AW172458, AA099207, AW205564, AW408650, AW205714, AA450308, AA636047, AI656442, BF437116, BE466112, AW575636, AW962721, AW206882, AA099221, AI620473, AA369585, AW469939, AW136836, BE547752, AI638262, BF059133, AA236642, BE551958, AW086133, AI917742, AI623315, AC005391.1, AL445584. 16.
HCWEB58	102	135241 6	1 - 1269	15 - 1283	
HCWGU37	103	104232 5	1 - 2763	15 - 2777	AV762098, AV718260, BG249643, BF677892, AI334443, AW965008, AV764228, BF697673, AI270117, AV710066, AI284640, AW072923, AV733830, AV713243, AL046409, BE646496, BF680074, AL138455, AW303196, BF241967, AW301350, AL037683, AL120483, AV760466, AV760599, AA055169, AA490183, AW406447, AV710387, AW769399, AA587604, BF681576, AI133262, AL046205, AI445582, AI281903, AW088212, AV764578, BF725504, AA244357, AI567674, AA521323, BF680041, AA813902, AV763354, AL041690, AV762645, AV763714, AV760042, AF330238, AA521399, AA719292, AV762959, AV759505, AV759204, AV760777, AW274349, AA838140, AA857486, BG167743, AV760937, AI307201, AI538852, AI696962, AA126035, BF676981, BE967369, BG109996, BF337291, AV762139, AL044940, AI963720, AV756693, BF679256, AV761286, AW472872, AV764530, AI672135, AV759172, AA501809, AV725431, AV761925, AW373587, AI076616, AW979060, AV762397, AI654588, AV728425, AW502305, AV760039, AV762050, AI431303, AV763670, AV762064, AV729809, AW518220, BE160727, BF668217, AI064864, BF679274, AA720702, AV763629, AA640772, AA526787, BE779948, BF311000, AW502100, AW963497, AA581903, AI204309, AF074677, AI679782, AV758946, AI917156, AV740801, BF684828, AW167799, AI133164, BG177715, AL042853, AI754955, AV735495, BF984050, AV764241, AV763385, AV764329, AI431232, AW950797, AW021583, AA569167, AA610491, AV682003, BF347791, AA488746, AV757607, AV725423, AW193265, AV710770, BF991286, AI471543, AI679294, AV763540, AA491814, AI538433, AU149045, AI623720, AW265385, AV759267, AU145239, AW473541, AW327868, BE049095, BF797630, AV763449, AV742057, AA837084, BF347740, AV761489, AI732865, BE146711, AI281881, BF965007, AI801482, BG236735, AW410400, AV760378, AL048626, AU155359, BE049139, BF673914, AI144055, AV760774, BF681427, AV761362, BF130605, N23097, AA470969,

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HCWKC15	104	553621	1 - 696	15 - 710	<p>AC006480.3, AL031429.11, AC005146.1, AC016830.5, AC020931.5, AC011489.6, AL049776.3, AC002487.1, AC002369.1, AC009516.19, AC005962.1, AC005523.1, AL133282.15, AL121658.2, AC009333.10, AC019181.4, AC010378.6, AP000783.4, AL132712.4, AL158830.17, AL391987.15, AL033383.26, AL137128.4, AL158052.10, AL590682.9, AP001718.1, AL354716.9, AL096840.25, AC006006.2, AL121897.32, AC022384.4, AC006965.3, AL354864. 16.</p> <p>AW504485, AI380617, AW805539, AV758903, AL079734, AA916430, AW819125, AV762982, AI625604, AI792575, AW084445, AW975210, BE138594, AW069227, AW023111, AV764259, AI792521, BE501593, AW021583, AI890324, BF725844, AW438542, BE138509, AV763026, AV763058, AA904275, AI521525, AA665330, BE077105, AA501461, AW969743, AW327591, AA535216, R94326, BF589824, AA574442, AW338179, AW271904, AI279417, AA651639, AI859946, AA524616, AW020150, AA833896, AV761862, AL042373, BE968744, AW004884, BF528591, AV760019, AA610509, AU131037, BF804385, AA833875, BF725761, AI053688, AI923052, AV761714, AI821714, AI792133, AI791913, AA013168, T74524, AI355246, AW474168, AI284543, BF724838, AI912401, AW068596, AV762633, AI564209, AW975626, AI620992, AI821785, AA483606, AV756220, AV754716, AA533176, BG236628, AI491765, H05940, BE139139, AA504906, AI250552, AA019973, BE049032, AA223174, AI798449, AA570740, BF965775, AL022238.1, AC006329.5, AL359402.3, Z98304.1, AC006948.4, Z84487.2, AC006312.8, AC026749.5, AC010627.5, AC008623.4, AC016656.5, AC016652.5, AC005531.1, AC004675.1, AC006057.5, AL033383.26, AL132768.15, AF088219.1, AC004849.1, AL031904.1, AC079177.21, AC007318.4, AL035659.22, AC074013.5, AC005829.1, AL035252.5, AL590762.1, AC005668.1, AC007216.2, U95742.1, AC005480.3, AF196969.1, AL158207.15, AC078846.2, AL121655.1, AC008754.8, AC011443.6, AC007191.1, AC008747.5, AL445217.3, AL161911.17, AC006515.7, AL034449.1, AI010597.1, AL031659.9, AC008891.7, AC016543.6, AL109628.5, AC009509.7, AB038653.1, AI400877.1, AF317635.1, AL160165.17, AC004106.1, AC004893.1, AL049776.3, AL121753.30, AC002553.1, AL132777.4, AC010530.7, AC005911.6, AL050349.27, AL158830.17, AP002815.3, AP001727.1, Z79996.2, AL035455.30, AL033529.25, AC087071.2, AC009501.3, AC007570.23, AL137229.4, AC004084.1, AC005746.1, AF314058.1, AP001717.1, AL365364.19, AC010463.6, AC004906.3, AC008044.4, AC022415.5, AC008848.7, AB001523.1, AC005387.1, AC007565.1, AC020904.6, AC091529.1, AC002316.1, AF283320.1, AL133163.2, AC026172.3, AL356113.8, AC005079.6, AL163210.2, AP001725.1, AF348209.1, AC002369.1, AC008784.6, AL161937.13, AC011481.4, AL354735.14, AC008622.5, AF111167.2, AC011890.4, AC006449.19, AL352978.6, L78833.1, AL096761.1, AC004593.1, AL096701.14, AL136300.22, AL121949.13, AL031432.1, AP001561.4, AC013355.7, AC090958.1, AL133153.3, AC005837.1, L47234.1, AC004448.2, AP000500.1, AC005840.2, Z95114.19, AJ011930.1, AL359091.10, AL163300.2, AC003101.1, AL139415.10, AC011485.6, AC007738.2, AC005225.2, AC002477.1, AC012306.11, AL035413.19, AC006146.2, AL109798.19, AL512347.14, AL109925.11, AC008762.6, AL355543.13, AC022468.5, AL162252.17, AP001753.1, AL121905.23, AC005283.2, Z98742.5, AL137145.13, AC006126.1, AL136039.4,</p>
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HCWLD74	105	628256	1 - 1526	15 - 1540	
HCWUM50	106	639037	1 - 1414	15 - 1428	
HCYBG92	107	598019	1 - 3047	15 - 3061	AW967979, AA937109, AA465498, AA465250, AW967765, AA262829, AA743297, H93605, AA325051, AW450216, H93604, AW206258, AU118507, BF513214, AW968591, BE934985, AA465142, AA309767, BE934984, AA204640, BE792699, BF795992, BG116852, AA765520, BF229206, BE838848, BE838830, AW499814, BE838839, BE163480, AU118047, AL158207.15, AF265550.1, AK000975.1, AB011126.1, AK001616.1, AK023681.1, BG258518, AL637633, A1948573, AW001026, BF194917, BE552379, AA614057, AI694037, AI697799, BF060693, AA978366, BE467885, A1948579, AI637607, AA614050, AW237074, AI656925, AW515719, N78018, AA398561, AI655689, AI681905, AI478149, BE549746, BE467846, H94848, AW235884, R71114, AW167543, AA393165, AW293106, AA621018, T79170, AI300825, AA628874, AA705305, T79253, N78013, AI130016, AI094422, H73384, AA682445, AA305338, W35200, BE464472, AW002908, AW205359, AI560194, H94906, AV726948, AW340784, AV725907, AV704971, R94883, AV704064, AV704660, AV726781, AV706814, AV706025, AV703342, AV727576, AV725152, AV707628, AV702984, AV726559, AV729411, AV706527, AV729593, AV706746, AV706910, R71180, AV652156, AV702071, AV706410, AA628873, H61723, AV729408, AV704245, AV703591, AV705525, AV652547, AV704304, H61929, AV705678, AV708423, AV707948, AV705174, AV704974, AV704378, AW271500, AV658362, AV703388, AV709514, AV729017, AI873386, AV702222, AV753858, AV707451, AV706290, AV659189, AV706395, AV703862, AV707769, AV705020, AV707510, AV706596, AV709356, AV725845, AV661744, AV725181, AV706357, AV705532, AV702637, AV726319, AV729129, AV705443, AV725431, AV708347, AV650367, AV706742, AV728884, AV703232, AV645768, AV702958, AV703453, AV706851, AV653845, AV712021, AV701626, AV705662, AV707882, AV727103, AV727347, AV704520, AV728715, AV709935, AV725369, AV682390, AV701985, AV726480, AV706047.

HDABR72	108	130151 7	1 - 1677	15 - 1691	<p>AV706925, AV726754, AV726392, AV725043, AV706891, AV651503, AV702187, AV714286, AV706724, AV707783, AV701657, AV702869, AV727583, AV727929, AV701728, AV701851, AV701611, AV728471, AV703417, AV702798, AV701875, AV703542, AV707798, AV706220, AV707117, AV728459, AV704924, AV708720, AV727355, AV704279, AV702639, AV724987, AV705234, AV705263, AV705282, AV702671, AV707589, AV729220, AV729357, AV725387, AV702673, AV701783, AV706104, AV701596, AV759156, AV693117, AV692972, AV705555, AV725956, AV728185, AV733476, AV702409, AV707685, AV702402, AV726532, AV706453, AV707686, AV702792, AV708809, BF590406, AV704605, AV726183, AV709692, AV705343, AV701538, AV725927, AV701496, AV707690, AV727189, AV725514, AV706318, AV703214, AV725281, AV729983, AV745940, AV726703, AV706394, AV703367, AV702537, AV707658, AV706889, AV725154, AV728289, AV707088, AV647654, AV702954, AV701499, AV703505, AV702787, AV706532, AV709932, AV702383, AV705504, AV701560, AV740894, AV704116, AV704611, AV703125, AV705273, AV704879, AV656240, AV706234, AV712350, AV725989, AV702498, AV727932, AV707171, AV705280, AV728872, AK000378.1, AC007182.3, AK027804.1, AJ244005.1, AJ244004.1, AJ244003.1, D78345.1, U94592.1, AJ244007.1, D50010.1, D13316.1, AB025273.1, AF144029.1, AJ276256.1, AJ276254.1, Z30183.1, Y14219.1, AJ244006.1, X82834.1, AF144028.1, AB005666.1, AJ276255.1, D88547.1, U45328.1, R17907, R17999, R71181, H16983, H58191, H73385, N58423, N58428, W23756.</p> <p>BE294597, AA749068, AJ284640, AL046409, BF677892, AW193265, AI431303, AL138265, AI334443, AV760777, AI613280, AV763354, AW419262, BF668217, AV760937, AI963720, AV740801, AI281881, AF330238, AI345654, AW502975, AV710066, AI270117, BG249643, AI305766, BF311000, BG109996, AV762098, AV734666, AW965008, AW576391, BF337291, AV762050, AV761362, AA610491, AW410400, AW833862, AL045053, AI345518, AL138455, AW327868, AV728425, AI350211, AW270270, BE047069, BF697673, AV735370, AW500125, AV764307, AV761489, AV762111, AV764578, AV762395, AA631507, AV725423, AV763255, AV763971, BF679304, BG222267, AA526787, AL044940, F36273, AA469451, AJ610159, AL041690, AV759274, AV761786, AL119691, AI305547, AA490183, AI754658, AV762139, AL037683, AI821271, BF241967, BG236735, AV757607, AI568678, BE350475, AV764241, AA491814, AW872676, AI708009, AA720702, AW472872, BG059568, AI053672, AW963497, AI133164, BF827410, AL042420, AW439558, AI289067, AW969629, AW974109, BG171096, AW438643, AI355206, BF681576, AL046205, AW276827, AV760774, AV762064, AV756693, AV652936, AL120687, BF130107, AI149478, AW975425, AV763633, BE049139, AA468131, AI471481, AV760042, AI688846, AV762959, BF854876, AV759505, AW269488, AV764398, AI537506, AV762397, AV763670, AV658688, BF940837, AV763195, BE154617, AW088202, AW407578, AI679782, AW630298, AV762535, BE872393, AI619997, AI341664, AI345681, AI345675, AI801482, AV733830, AF074677, AW406162, AW103758, AV763540, AV762154, AW193432, BF475381, BF964720, AA623002, AI375710, AV682003, AV759382, AV757425, AW083402, AI633025,</p>
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HDHEB60	109	499233	1 - 1407	15 - 1421	AL524364, AL527936, BE729676, BE734215, BG034535, BE879791, BG030700, BE782405, BG031399, BF219970, AW961043, AW245732, BE540977, BF125197, BE264862, BE264047, AA523441, BF348672, BF125434, AW250195, AW860381, AW246993, AL654715, AW168308, AI949310, AW068175, BE259690, AI393119, AW938768, BE279977, AW938746, BE857719, AW190234, AI871661, AA494392, AW900867, AA338903, BG006350, AL527587, BF091980, AA602247, BF804618, AW364083, AA357684, AW178944, R40832, BF374357, AW662637, AL524365, R42008, C20713, BF360339, BF915537, AW088134, BG035330, AI800433, AI559667, AI800453, AI536557, BE907440, AI689463, AI922091, AW151136, AI498579, AI539771, BE897632, AI432644, AI952433, BF914091, AW118557, AI926593, AW151136, AI498579, AI539771, BE897632, AI432644, BG254284, BF304748, AI537677, AI494201, BF812963, AI500659, BG180468, BE883591, AI868831, AI866465, AI815232, AI866691, AI801325, BF812438, AI500523, AI538850, AW089221, BE968552, BE885490, AI887775, AI582932, AI590043, AI284517, AI923989, AI872423, AW172981, AI500706, AI445237, AI491776, AI289791, AW151138, BF811804, AI521560, AI889189, AI500662, AI582912, AW172723, AI284509, AI539800, AI889168, AI440263, AI538885, AI927233, AI866573, AI633493, AI434256, AI866469, AI434242, AI805769, AI888661, AI284513, AI500714, AI888118, AI277008, AI285439, AI436429, AI859991, BE964045, AI355779, AI623736, AI889147, AI371228, AI581033, AI431307, AI440252, AI491710, AI440238, AI047422, AI866786, AI567971, AI610557, AI860003, AI539707, AI885949, AI285419, AW089557, AI559957, AI521571, AI469775, AI866581, AL047398, AW074057, AI815150, AI567953, AI446495, BE906230, AI867068, AI225248, AI698352, AI815239, AI371229, AI921420, AI624279, BF913616, BG252929, AI701890, AI687614, AA464646, BF038804, AI919345, AW858243, AI282249, AI962040, AI829330, AW078839, BE895765, AI554821, AI561170, BE764656, AI636811, AL515375, AI500146, AL042365, AW059765, AI263331, AI610756, AI440260, AI690946, BF814072, AI890907, BF811802, AW129310, AI866458, AI431238, BF815930, AI648567, BF925348, AL514069, BE540578, AA830821, AI924051, AI433157, BE964497, AI273179, BE621206, BG108452, AI371251, AI866510, AI499986, BE968711, AW151974, AW073697, AI866461, AI923046, BF339011, AI049859, BF752892, AI436458, BF526393, AI379711, AI918408, AI334445, AW169643, AL048403, AI915201, AA878808, BF764538, AI349814, AI953880, AI702902, AI800171, BE881675, AI819663, AI432656, AF118240.1, AB016531.1, BC000467.1, BC004356.1, BC000632.1, AK025906.1, BC004937.1, AK027081.1, BC007634.1, AL133070.1, X79204.1, AK000247.1, BC004908.1, AL080162.1, AL136781.1, AF017790.1, Z22828.1, U92992.1, BC002356.1, BC008382.1, BC001093.1, AL080127.1, AL136748.1, BC008195.1, AB048910.1, BC000713.1, AK024550.1, BC008818.1, BC001470.1, AK027116.1, AL133084.1, BC008488.1, AB063077.1, AL137275.1.

HDHIA94	110	765171	1 - 1475	15 - 1489	AF056191.1, AK026086.1, BC004370.1, AB047609.1, BC003105.1, BC006164.1, BC002485.1, AL122098.1, AF111847.1, BC008893.1, M92439.1, AP001343.1, AL512454.6, BC002839.1, AK026038.1, AJ004832.1, X72889.1, BC002491.1, AK026865.1, AK026021.1, AK025084.1, AK025958.1, BC002607.1, AL136825.1, AL133049.1, BC001790.1, BC000785.1, AB060905.1, AL161953.1, AL136765.1, S77771.1, BC004926.1, AL137429.1, BC006207.1, AL389978.1, BC006508.1, AF067420.1, AK026642.1, AK026590.1, BC007657.1, AF260566.1, AB063087.1, BC002844.1, AF369701.1, BC004181.1, AL117432.1, BC000511.1, BC000386.1, BC007852.1, AK026749.1, AF151109.1, BC005805.1, AK026164.1, AB049629.1, AK025092.1, BC008717.1, AK026627.1, AL161802.15, AL353745.7, BC008365.1, D83989.1, U80742.1, AK026648.1, BC007207.1, BC002495.1, BC009272.1, AL136763.1, AL137556.1, AL136540.1, BC002777.1, AL080154.1, AK026532.1, BC009284.1, AC004690.1, AK026389.1, AF353396.1, AF022813.1, BC001328.1, BC002816.1, AL049423.1, AL049314.1, AB060837.1, AL512705.1, BC002524.1, AL137536.1, AK025541.1, AF036268.1, AL080126.1, AL389935.1, AK026631.1, AC044797.5, AK024622.1, BC009212.1, BC005007.1, S61953.1, AB019565.1, Y10080.1, AK025391.1, AK000432.1, AK026522.1, BC004265.1, AK026541.1, AK027161.1, AB047941.1, AL157464.1, AK026793.1, AB060929.1, BC008785.1, AK025431.1, AK026603.1, AB060839.1, AK027142.1, AL137656.1, AL133565.1, AL137665.1, AJ406932.1, AC003032.1, AC005057.2, AC010137.3, AL353802.14, AC005968.1, AL157360.8, AL162713.19, AL359997.8, AC007298.17, AL133629.1, BC006332.1, BC003687.1, AF030165.1, AL122100.1, AL133053.1, BC002476.1, BC000066.1, BC003122.1, BC006133.1, Y00093.1, AF002985.1, AB055805.1, AL122049.1, BC009395.1, BC002519.1, D44497.1, BC000377.1, BC001963.1, BC001191.1, AB060226.1, AL137557.1, AK000655.1, AF218023.1, AL162062.1, AK027188.1, AF188698.1, BC006412.1, AF218034.1, BC006465.1, S76508.1, AK027868.1, AC021020.3, AL080158.1, BC000317.1, BC005854.1, BC008025.1, U67211.1, AL050138.1, X99226.1, U77594.1, BC001082.1, AL110159.1, AF169154.1, AF271350.1, AL080060.1, AL136884.1, AK027114.1, BC002647.1, AB050418.1, AK025209.1, AB049758.1, BC004119.1, AL157431.1, AL137660.1, BC008078.1, AB056768.1, AL080129.1, AL110222.1, AL136882.1, AF205073.1, U51587.1, AL135933.1, AL157878.1, X66417.1, AL035458.35, BC006487.1, BC006147.1, BC003651.1, AF358829.1, BC007280.1, AK000445.1, AK026571.1, AL512746.1, BC002386.1, BC006198.1, S69510.1, AF112208.1, AF124728.1, AL162085.1, AF321617.1, AL137662.1, AL137480.1, Z94277.1, AC006222.1, AC010088.3, BC001427.1, AK026591.1, BC004960.1, AK000450.1.
HDHIA94	110	765171	1 - 1475	15 - 1489	T75217, R21117, F12855, AA825244, T06656, AA393627, AA400803, BF087642, AF169257.2, AL121761.5, AL121830.25.
HDHMA72	111	547772	1 - 4449	15 - 4463	AF107454, AU131474, AL527406, AL527364, AL525109, AU125391, BF969516, AW207619, BE908862, BF968132, BG260993, BE876744, BF439992, BF667287, AW340566, AA534290, BF130397, AA282393, AI635585, BE857014, AW953405, BF132394, AU145369, AA776464, AW139543, AI880884, BE874401, H24404, AI564770, BE618887, AA205320, AA307511, AI697902.

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HDLAC10	112	692299	1 - 1463	15 - 1477	<p>BF222902, BE908203, AL049012, AV751505, BF589784, BF939631, AV752758, AW161772, BF984735, BE156564, AI963569, AI627938, AU145766, AA430167, AW885969, AW885971, AU144116, AW885970, AW150904, AA811288, AW148833, AA016001, AU146932, AA534493, BE246689, AW572295, BG260240, AU155669, AI580793, AU149721, BF791136, AI473859, AU157762, AU150899, AU119418, AU150032, AA552599, BE349918, AI762820, BF572303, AA630256, AI249503, BE348915, BG257768, AI289630, BF941915, AI093700, AI683179, BE767826, AA902142, BE243543, R50658, AA994326, Z43651, AW589235, AI796343, Z39714, BE246512, AU156488, BE246684, BF184442, T36201, R50558, D60811, BE247745, BE165921, AI796404, AW023060, AI560541, AA445981, Z45738, BE242535, BF693665, AV657085, F04619, BF692774, AU121025, AW960825, BF571603, AK025407.1, AK025829.1, AF205600.1, AF205601.1, AK022942.1.</p>
HDLA028	113	890457	1 - 1970	15 - 1984	<p>BF669871, BF516590, BE891179, BF674702, AW968749, AA521300, BF034206, BF699497, BF218327, AI567665, AI749981, AA947871, AW968575, BE645523, AA812212, AA173660, AA669111, BE672554, AA279266, AA236768, AI139058, AW956031, BG178790, AA826451, AI281579, AA173659, AA737682, AA769373, AA156985, AA156679, AI263368, AA625733, AA491131, AI367576, AA236924, AA767739, AI281500, AA669931, AA279289, AA251939, AW304714, H78481, AW193270, AA136483, AA669955, R21922, H03284, T56019, R22571, AA223255, H03285, AA032147, AA032146, R25418, R28446, AA369930, AI289500, AA199609, AA095606.</p>

HDPB132	114	135236 0	1 - 1499	15 - 1513	BF317233, BF348587, A1886854, BE262234, BF347922, A1564810, A1571772, BE260801, BF947408, AA620986, AW964855, BF348199, AL118922, A1948418, BF590647, AA682932, A1197966, W56893, BE832972, H38493, AW139827, AA984436, H49766, AA604007, AA324912, H38543, BF959580, A1816315, BF957744, H30751, H38473, A1565716, AW160990, A1027311, AA326240, BE383259, A1369823, R88620, BF928045, AA323285, AA326352, BF445694, AW904314, AW964663, BF957741, AW896684, AW896682, AW875497, BF758599, H51158, AW896689, AW904318, R89653, BE702414, R85211, AW888897, A1468058, BF206086, R88824, AW904306, R88628, H51120, AW896674, H41534, BF967275, AA622175, BF947811, AB023167.1, BC000051.1, AF190461.1, AB060204. 1.
HDPBQ71	115	116031 6	1 - 2298	15 - 2312	AL517702, AL535136, AL517701, BF966919, AV712906, BF310001, BE785105, BG023779, AW608043, AW959115, AW571652, BE546297, AV733133, BG164317, BF965688, AA910337, AW070547, AA630221, AA936329, A1077660, N66596, AA233825, BF769251, AW169158, BE896148, AW966447, A1092899, A1804163, BF966148, A1184325, A1400074, AW105140, A1038519, BE178803, A1243767, A1803580, AA449258, A1089365, A1969422, A1292304, AA971310, A1753091, AA233729, A1289889, A1335939, A1275621, A1748056, BF828492, AA451735, AA973548, H19041, AW129980, BF791539, AW472838, H65681, AV748196, AA666224, BF940460, A1002830, A1374721, A1264277, H29405, BE930289, AA446666, R52737, N99048, F06358, AA233772, H11875, H65682, BF725919, R64291, R59440, AA812450, Z44951, BF825554, BE711465, F07390, AA093749, A1080343, R24935, R64256, AA878276, BF248328, AA081567, AA081513, R20695, D11945, AA249453, AW630557, AA331924, F07956, A1672272, AA383930, AA385881, R63983, AA865796, A1078076, AW964475, AA448551, BF878091, BF091153, T97552, AA453075, BE937893, N98627, T53666, BF836787, R64175, R63901, AA319203, AA424168, BF791814, BG001790, H11513, BF376043, W30696, BE739183, BF086020, BF376012, AW189731, BF769066, AA383577, AW388471, AW388477, AW810765, AW388507, BF247577, AW810647, AW810736, AA092943, T97598, AW810677, AW627523, AW810964, A1261898, BF216270, BF855391, AW810687, A1221448, A1147974, A1611624, AA730133, A1377784, A1672529, BE551587, A1936568, BF115500, BE466653, AW303619, AW388498, BF382656, BF751597, A1962331, AW006254, A1351767, A1655026, AA884783, AL119457, AL119324, AL134524, AW971745, BE161864, AW149892, AL119396, AL119443, AW804686, AW392670, AK027596.1, BC006321.1, AF212247.1, AB062962.1, AC007533.2, AB026436. 1.
HDPCJ91	116	740748	1 - 6093	15 - 6107	AU119059, AW959367, BF792861, BF672087, BE439439, BE717153, BE770928, BE718895, AW971539, AL079949, BE770941, BF687684, BF132755, BF727151, BG009815, A1703121, A1066742, BE968461, BE717019, AW444843, W61007, A1949993, AW502324, A1150343, A1859085, AA393478, AW467411, BF515251, BF063545, BE717046, BE042969, BE673935, AU154204, AA292253, AA838717, AU145486, A1273190, AW512776, BF727150, A1084372, A1597583, A1457829, H99255, AW474793, BE327577, A1697937, A1167388, A1684736, W69563, W31042, AW753588, N98496, A1307397, AW613687, AW241267, BF198110, W60918, AA291214, AW316965,

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HDPCO25	117	460682	1 - 753	15 - 767	AI193249, AI809829.
HDPCY37	118	837699	1 - 1918	15 - 1932	AL520370, AL529690, AL524481, AL520369, BE274454, AU141822, AU132723, BF314732, BE273689, BF026599, BE736766, BE791870, AI191318, BF689450, BE894541, BF690012, BF344946, BE880507, BG118146, BE410790, BE620315, BF969947, BE908116, BF183246, AW239293, BE260297, BF983977, BG121624, BE293262, BE907076, BE620852, BF868566, AI978812, BE049271, AA586860, BE272490, BF034205, AW474556, BE293363, AA805184, AI628509, AI582366, W73797, BG118530, W73745, AW083832, AI620297, BF434062, BE293362, AW967627, BG120472, AW628388, BF690389, AW513995, AI056600, AU154200, AW386876, BG166073, AI056739, BG253585, AI362766, AI494212, AI077551, AV711723, BF689649, AA935678, AI348675, AI358232, AA251769, AA968828, BE788883, BG252031, BF846596, AA659758, AI891139, BE964553, C06060, R67182, AA746268, AA506524, AA251926, AV736190, D81244, AA291462, H58621, AV739502, H58622, BF690549, BF183479, R38144, AI919497, AW193598, AI250032, AV740386, AA604444, BF359113, AI567397, AA905208, BF880393, BF745974, AA836253, R57498, AI525934, BG107079, AW663025, AW754473, BE718998, AA551675, AI364618, AI421662, BE938093, AW166086, RS9996, AW151132, AI469754, AI554821, AL042593, AI654286, AL513693, AL513991, AI366900, AL515171, AW858522, AW151974, AW058275, BF970652, AL043152, AL513823, AI815239, AL513569, AV681993, AI538850, AI513713, AI801286, AL514919, BF033177, AL513729, BF304021, AI271716, AI815233, BG167830, AI440260, AI537677, AI494201, BF812963, AI804505, AI500659, AI513901, BE883591, AI866465, AI815232, AI801325, AI866691, AI500523, AI887775, AI582932, AI590043, AI923989, AI284517, AI872423, AI500706, AI491776, AI445237, AI289791, AI926593, AW151138, BF811804, AI889189, AI521560, AI285417, AI500662, AI623302, AI924051, AI539800, AI582912, AI284509, AW172723, AI538885, AI889168, AI440263, AI927233, AI866573, AI633493, AI434256, AI866469, AI434242, AI805769, AI888661, AI889191, AI500714, AI284513, AL514043, AI888118, AI285439, AI859991, AI436429, AI355779, AI623736, AI889147, AI581033, AI371228, AW194509, AI491710, BC001371.1, AK002393.1, AK001645.1, AY007088.1, AL135844.9, AF086313.1, AL356652.19, AL162002.1, AF155656.1, AF326206.1, AF265236.1, AL022315.1, AF084644.1, AF084645.1, AF159615.1, AL133084.1, AL133655.1, AL136805.1, AL133076.1, BC009395.1, AL136763.1, AL133047.1, AL133051.1, AL137561.1, AL133070.1,

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HDPFB02	119	898208	I - 3422	15 - 3436	AL521596, AL521595, AL537690, AL537691, BG164147, BG260349, AW579704, BE787742, BF339441, BE147943, BG251728, AV704431, AW370664, BE148069, BF570111, BG027543, BG110212, BG030218, BE148079, BE874591, BG104640, BE706255, AW748481, BF984597, BF836429, BE539121, AW936159, BE147942, AW370670, AW937902, AW605173, AW370668, AW373397, AW370689, AW370665, AW937893, AW608803, AW937904, BE147980, AW608712, AW937888, AW937890, BF830716, AW379040, AW972283, AW972281, BE261966, BE048242, AW370674, BE148065, BF830631, AI084729, AW875470, AW370671, AI476782, BE620122, AW608713, BG170475, BG105828, AI675360, AI609081, AW370661, AA447617, AW972288, AI660011, AA448014, AA905682, AA194120, BF839878, BF345038, BF839879, AW580410, AI804395, AW875465, AI806699, BF195101, AI471976, BE148063, N51375, AW608829, BF840328, BE208162, AW390807, N30496, AA130156, AI298278, AI683457, N26284, BE019800, AI419725, AI368909, BF349972, AI683317, AW181901, BE312529, AA742660, AI520668, AW580406, AW083044, AW370662, AA057838, AI084876, N54338, AI806265, AA627446, AI587194, BE147996, AI928281, AA494093, AI928536, BF851601, AW608708, BF525869, AW338382, BE717999, BF105926, AA223133, N39463, AI364557, AI092740, AI675922, AA736412, AA687735, AA862124, AW378681, AW117328, BF998867, BE787979, BE882684, W52184, BE147993, AI094023, T69559, AA130120, T77734, H82591, AA295128, AI005397, AW753575, BE093237, T71295, AA227005, BF734572, AI372948, BF978965, H44297, T71435, AA478215, AI074980, AI088215, R11436, BE147828, W31197, AA934070, AI589134, AI421523, AW390780, T69625, AA903765, BF365447, BE147934, N21264, AW088052, BF741721, AA194011, AI831663, AW769622, BG236830, AW375570, AW665361, AA903763, AW771721, AW088044, AW339928, BF772279, AW663074, BE740207, BF355612, AI273022, AA935625, AA458984, BE763203, AI866457, AW875610, AI814594, AW383043, BF840329, T77735, BE147829, BF356464, AA478053, AA922987, BE906866, AI926333, AW875534, AI569429, AW192687, BF798292, BF859018, AW375699, BF762165, BF821121, AI818581, AW827211, AI475371, AI436456, AL121365, AW071349, AI538716, AV756122, AI687728, AL513907, BE047863, AV757455, BF883916, AL514627, AI433157, BF793644, BF970162, AI702406, AW268253, AI349772, AV732936, AI818683, BG257535, AI064830, AL047763, BG109270, BG031815, AI499393, AV711509, AL036146, BG179993, BE785905, AL047042, AL121270, BE881061, AL045500, BF812933, AV727776, BG151247, BE048071, AL513553, AI580190, BF054789, AL515041, AW827203, AI934036, AL513597, AI758437, AL360136.1, AF302102.1, AL360144.1, BC008417.1, BC008365.1, AL442082.1, AL512733.1, BC008488.1, AF090903.1, AL050393.1, AL133640.1, AF090900.1, AB055303.1, AL117457.1.

				AL136586.1, AB048953.1, AB056420.1, AL117460.1, AF090934.1, BC008387.1, AL110221.1, BC007021.1, AL049452.1, AF090943.1, S78214.1, AF104032.1, AF078844.1, AF090901.1, AJ742859.1, AL359601.1, AL133606.1, AL136787.1, AL133016.1, AL050146.1, AL442072.1, AL080060.1, AL157431.1, AF125949.1, AL389978.1, AL110196.1, AF218014.1, BC003687.1, AL359596.1, AL137527.1, AL049938.1, AK026608.1, AL390167.1, AK000212.1, AB060916.1, AB049758.1, AL136892.1, BC003683.1, AL049314.1, AK025339.1, AF111847.1, AB056809.1, AL122050.1, AB060887.1, AB063046.1, AL050149.1, BC001967.1, AL136749.1, AB063070.1, AL136789.1, AL162006.1, AK026741.1, AK026865.1, AF090896.1, AB048964.1, AL133075.1, U42766.1, AF106862.1, AL050116.1, AB050510.1, AB047615.1, AK025084.1, AB047801.1, AK027868.1, AL162083.1, AL050108.1, AB055361.1, AB056768.1, AK025958.1, AL080137.1, AB060908.1, AB019565.1, AL049466.1, AK026045.1, BC006807.1, AB063008.1, AL096744.1, AL122093.1, AL137283.1, AL050277.1, AK026744.1, AL133557.1, AL136799.1, Y16645.1, AF219137.1, AL389982.1, AL117394.1, AL080124.1, AK026855.1, AK000614.1, AL133080.1, AL136768.1, BC002733.1, AL137557.1, AL137459.1, AL133093.1, AL136844.1, AL133565.1, AF097996.1, AB060912.1, AK000618.1, AL1512746.1, AK027096.1, AL049430.1, AB060863.1, AK025092.1, AL122123.1, AL122121.1, AK026927.1, X82434.1, BC004556.1, AB062938.1, AK027113.1, BC006195.1, U91329.1, AL359941.1, AL353940.1, AF146568.1, AK026647.1, AL1512718.1, AK026542.1, AF091084.1, AL137550.1, AK026533.1, AK026784.1, AK025772.1, AL1512719.1, AL359618.1, AL1512754.1, AK000137.1, AK026452.1, AF125948.1, AK000083.1, AF207829.1, AK026534.1, AB048974.1, AF271350.1, AK026583.1, AB053368.1, AL050138.1, AK026592.1, AB048954.1, BC001045.1, AL110225.1, AB060826.1, AB060852.1, AB060825.1, AL049382.1, BC004951.1, AK026532.1, AK026959.1, AK000445.1, AB055315.1, AL117435.1, AL133560.1, AF225424.1, AK000652.1, AB052191.1, AL117583.1, S61953.1, AL049464.1, AB051158.1, AB055366.1, AK025491.1, AK026504.1, AL050024.1, AK025414.1, AL117585.1, AL137271.1, BC008070.1, AK026086.1, AK024538.1, BC008899.1, AF177336.1, AP001873.3, AL049300.1, AK026480.1, AK000323.1, AL1512689.1, AL136845.1, AB047904.1, AF183393.1, AK027164.1, AL359615.1, AK026528.1, AL136786.1, AL122098.1, Z82022.1, AK025391.1, AL359583.1, AK026353.1, AL136928.1, AK000432.1, AB056421.1, AB063093.1, AK000647.1, AK025967.1, AB052200.1, AL133258.16, AL359622.1, BC007199.1, AB049892.1, AK026642.1, AL122110.1, AK024524.1, AK000718.1, AC002467.1, BC002839.1, AK027204.1, AF260566.1, AF348209.1, BC008382.1, BC008485.1, AL353802.14, U80742.1, AL130156, X72889.1, AL049283.1, AL133113.1, AK025209.1, BC006525.1, AK025484.1, AK027116.1, AC007390.3, AL157482.1, AF061943.1, AL137538.1, AL133072.1, AK025524.1, BC008280.1, AL137463.1, AK026947.1, AL1512684.1, AB055374.1, AC026464.6, AC022215. 4. AL526869, AL523945, BE794829, AL532486, AL533032, BF969304, BG115956, AL514521, AI871493, BG028151, BF689553, AL531509, BF689896, AA005246, AW392303, AI921136, BE620088, AI921426, AL514522, AI800003, AI571833, AI097128, W68743, AA587786, AI928547,
HDPFF39	120	588697	1 - 1242	15 - 1256

					<p> AI588884, AI366187, AI469283, BG059843, AI091266, W68721, AA731294, AI023709, BE218286, AI571471, AI628000, AI819634, BE207917, AI247849, AI085331, AW274586, AI752152, AI866693, BE382434, AW264556, AI570330, AA09256, AW602670, BF091955, AI185842, AI627586, AI189900, AI417779, BF822519, BE673374, T81959, AI623337, AI970967, R86832, BE940065, AA074519, BF944761, AW364990, AA865886, AA722301, AI539598, BF095254, AI494220, AA327238, BF345347, H82580, AI571973, AW516484, T81955, AW439461, R56100, W27475, AW470712, BE743030, AW674734, AI953321, AA076557, AW73075, AW365079, BF056789, AI134661, AW131498, AW772519, AI609719, BF855458, AW073075, BF799596, BE938387, AW517642, AW886746, R60226, AI918145, T57354, BG253820, BE886275, BF799596, BE938387, AW517642, AW886746, BF951584, BF684157, AW204188, AI032686, BE936805, BE843795, BE933378, AL523946, BF999019, BF980469, AI589371, BG120896, H16171, BE937970, AW938898, T57436, AW882041, BG121424, BF851425, AL532487, BG163558, BF762612, AW138659, AI364407, AW513032, BG105148, AA005140, AI097132, AA767618, AI572822, R86655, BE962190, BF947166, Z43259, BF690126, BG115718, AW663033, AI932620, AI559976, BE620628, AI358271, BG167830, AI924051, AW858522, BF812963, AI804505, AI500659, AI815239, BE883591, AI866465, AI446536, AI815232, AI801325, AI866691, AI500523, AI538850, AI887775, AI582932, AI872423, AI590043, AI923989, AI284517, AI500706, AI491776, AI445237, AI926593, BF811804, AI289791, AW151138, AI889189, AI521560, AW151974, AI500662, AI785417, AI623302, AI539800, AI284509, AW172723, AI582912, AI538885, AI440263, AI889168, AI927233, AI866573, AW058275, AI567961, AI633493, AI434256, AI866469, AI434242, AI805769, AI888661, AF037339.1, AK027698.1, AF037338.1, AC011489.6, BC004865.1, AL133655.1, AL133074.1, AL136763.1, AL133076.1. </p>
HDPFP29	121	628254	1 - 1043	15 - 1057	<p> AW575379, AA769318, AI796662, BG029535, AW269780, AA809133, AA427866, AW953923, AI419264, AW088714, AI400326, BF945261, AI924874, AI150755, AI623762, AI239506, AI619494, AW148696, AI797909, BE327745, AI634907, AW070513, AI186243, AA768972, AA804195, AW674541, BE221186, AW204520, AA292638, AA235326, AW341643, AI005076, AW004816, AW603880, AW007235, AI871816, BE826643, BF222941, BE826639, BE826631, BE826634, AA292639, BE826687, AW514133, AA627727, AI690331, T05561, AW405407, AI673409, BF814220, AW075831, AI923685, AA931499, H56443, AW083896, BG165971, H56444, H16157, T82850, AW131313, AI249783, AA714383, AA548622, AI810663, BF091047, AA810885, R51826, F21597, AA702095, AI832872, AA832395, BF974513, T34785, AA524210, T16401, T90272, R28256, BE826642, AA262993, BF903485, AA568882, AW075840, AA535317, AI909659, R28033, BF814542, AW970732, AI810273, AI262373, BF000060, AI927452, AI679783, AI272283, BF901241, BE559850, AA742649, BF900830, AA922242, AI439758, AI445719, AI738794, AI625812, AI215105, AA749066, AI275641, BG054585, AA527826, BE143233, AA525108, AI950316, AL522808, BG111850, AA643261, AI432644, AI927233, BF771135, AA033725, AI699011, BE883591, AI431307, BG110517, BG113493, BG029667, AI433157, AI648567, AI690946, AI554821, BG252929, AW151136, AI539771, BE897632, AI537677, AI494201, BF812963, AI500659, AI866465, AI815232, AI801325, AI500523. </p>

					AI538850, AI887775, AI582932, AI590043, AI872423, AI284517, AI923989, AI500706, AI445237, AI491776, AW151138, BF811804, AI932949, AI521560, AI889189, AI500662, AI539800, AI582912, AW172723, AI284509, AI538885, AI889168, AI440263, AI866573, AI633493, AI434256, AI866469, AI434242, AI805769, AI888661, AI500714, AI284513, AI888118, AI285439, AI859991, AI436429, AI355779, AI623736, AI889147, AI371228, AI581033, AI491710, AI440252, AI866786, AI610557, AI860003, AI242736, AI828574, AI887499, AW151979, AI539781, AI539707, AI702065, AI885949, AW089557, AI559957, AI285419, AI521571, AI469775, AI866581, AI815150, AI567953, AI446495, AW858243, BG164558, AA806719, BE885490, AI289791, BF811802, AL110306, AI929108, BG257535, BC027628, BF338002, AL045500, AI866820, AL042515, AI561170, BE886728, AI784028, AI890907, AL039390, BF795712, BE895765, BF815930, AI468872, BF802671, AW089006, BF812438, BG260144, AI371251, AL079960, AI866510, BE047852, AI274759, AI866461, AI923046, AI565172, AL047422, AI431316, AL048403, BG168086, AW827227, AA074168, AI433976, AI867068, BG113224, BF725463, BE537531, X79568.1, U28282.1, AK027136.1, AC007383.4, BC006408.1, AB060841.1, AL110280.1, AC026464.6, AL133049.1, AL137294.1, AC023880.5, BC006159.1, BC004431.1, BC008078.1, AC010149.8, AK025209.1, AK026793.1, AL080124.1, AL389935.1, AL137271.1, AC006994.4, AC021325.5, U72621.3, AC016652.5, AL359620.1, AL035458.35, AL133014.1, AF012536.1, BC008417.1, BC001844.1, AL137538.1, AC004987.2, U77594.1, AC008592.4, BC006136.1, AL136843.1, AC011450.4, AL353625.5, AF090900.1, AK026626.1, AC018643.3, BC007998.1, AL137705.1, AB060826.1, AL080234.1, AK026894.1, BC002355.1, AL390154.1, AL136766.1, AL137292.1, AC009087.4, BC008708.1, AL137530.1, BC008280.1, AK027160.1, AF095901.1, AL133344.28, AL353999.3, AC004822.1, BC009395.1, BC002473.1, AL136845.1, AB060888.1, AB060229.1, AK000432.1, AC004686.1, S77771.1, AL353802.14, BC006509.1, AF334404.1, BC009026.1, AL355834.4, AL353594.13, AP001873.3, AL356278.8, AK027217.1, AK025632.1, AK024546.1, AL133104.1, AC005902.7, AK000655.1, AK024747.1, BC000714.1, AK000647.1, AK025484.1, AF056191.1, AF348209.1, AK027161.1, AF120268.1, BC009355.1, AK000391.1, AC006313.1, AL122049.1, AF353396.1, AB063070.1, AK025015.1, AB047631.1, AF179633.1, BC004215.1, BC004908.1, AB056768.1, AK025465.1, AL137665.1, AB060842.1, AL391244.11, AK000450.1, AL512684.1, AB049900.1, AC009484.3, Z82022.1, AF218006.1, BC002343.1, BC006494.1, AK000250.1, AL136768.1, AK025708.1, AB047904.1, AL157360.8, AK025383.1, AL161628.9, AK026591.1, AK000718.1, AL163282.2, AK024992.1, AL136622.1, AL137557.1, AL389978.1, AF285836.1, BC002519.1, AC006112.2, AF225424.1, AB060856.1, BC007460.1, AB055352.1, AK000212.1, BC007571.1, AC010530.7, AB055303.1, AB047869.1, AL137711.1, AF090886.1, AB060887.1, AF274348.1, AF274347.1, U80742.1, AL133619.1, BC006412.1, AL353807.18, AL136784.1, AL137476.1, D55641.1, AK026542.1, AL080060.1, AK026057.1, AK027193.1, AL136781.1, AF002672.1, AL356747.18, AL133560.1, AK026408.1, AF094850.1, AL359941.1, AF003737.1, BC004945.1, AC004383.1, AL136850.1, AB047966.1, AC010972.3, AL359600.1, AB060837.1, BC006180.1, AF132730.1,
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HDPGI49	122	785887	1 - 2669	15 - 2683	<p>AL137574.1, AL353745.7, AL162062.1, AF205861.1, AL121601.13, AL136892.1, AL050138.1, AL445236.22, S76508.1, BC004533.1, AF169154.1, AC024247.4, AC004883.2, BC009033.1, AL035407.15, AL138976.5, AE006462.1, AF151109.1, AL138770.3, AB055374.1, AL136844.1, AB056420.1, AF113222.1, AL512689.1, BC006411.1, AL137256.1, BC007198.1, AL122118.1, AJ012755.1, AL035587.5, BC007031.1, AF271350.1, AK027111.1, AF078844.1, AL132985.4, AK026533.1, AC006222.1, AL117463.1, AF245044.1, AC020659.5, AK024601.1, AF069506.1, AL022165.1, AB047878.1.</p>
HDPGP94	123	823355	1 - 3867	15 - 3881	<p>BG028956, BF434796, W05746, AW965426, BF509507, BF680194, BF589350, AA287841, BE697901, BE697902, AI032342, BE856794, BE251894, AI342589, AA218952, AW771921, AW118336, N24868, AI301200, AA761846, BF247512, AA911724, AV712358, AA831097, AA040238, AA809475, AA287842, AA252943, AI610808, AA040239, AA422118, AA235003, BF477762, D80028, AA985566, AI051755, AA450350, AI267777, AA768011, AA463666, H96432, AA411233, BE218411, AA332252, AA995400, D81515, AA974489, AA507522, AA653950, BF087088, BE242538, BG005055, AA249308, BF971120, AA487000.</p>
HDPGP94	123	823355	1 - 3867	15 - 3881	<p>AI382347, BE672925, AA328438, AI933550, AV658526, AV659132, F17041, AI378966, AW881484, AU159276, AI457143, BF435633, AL118834, AA299156, AW468555, AI926394, BF727445, BF689260, AI610326, F18611, BF878671, N26697, BF438919, R92170, AA069204, T78609, T62932, AV685376, AI928570, BF850110, T78394, AV718691, AV719171, AI220812, AI193408, AV720907, R84298, AV718419, AI309322, AA826143, F17026, AA724610, AI862212, AI439415, AI890953, H01156, AA347740, AA565837, H49709, AA811111, AL043725, AI147839, F16584, AA904946, AI054162, AA771958, AL570164, BF112065, AA132716, AW604787, BF679645, T06365, AI591332, AL137072.8, AC025097.41, AC016689.3, AC026951.5, AP003117.2, AF274857.1, AL096705.12, AL137881.12, AP001960.2, AP003534.1, AL049564.10, AC023134.5, AL109659.20, AC012450.9, AL133247.1, AL139093.11, AC079906.15, AL513163.8, AC015729.9, AC083865.2, AP001880.4, AC009501.3, AL390027.11, AL359545.12, AC016568.4, AC006313.1, AF250841.1, AP000810.5, AL160052.21, AC010980.8, AP001858.4, AC020717.3, AL139395.6, AP001831.4, AL109759.4, AL158069.16, AC004010.1, AL050309.4, AC002381.1, AC090497.2, Z84720.1, AC017089.3, AL136136.7, AC003051.1, AL049835.3, AC007436.1, AC004384.1, AL158150.14, AC006362.2, AC008817.7, AC008582.6, AL356317.8, AE000661.1, AC007486.1, AL160236.4, AL132800.4, AL358274.3, AL590043.7, Z68871.1, AC025254.14, AP001712.1, Z93019.1, AC004855.1, AP002532.1, AL360157.12, AC008664.5, AC007253.2, AF003529.1, AC018927.6, AL445523.11, AC022443.4, AC004385.1, AC009483.3, AL359400.4, AC009779.18, AC016579.5, AL390039.10, AF280107.1, AC008550.4, AC023426.29, Z84474.1, AL080312.14, AL121788.17, AC021998.4, AC073574.11, AC012669.7, AC005342.1, AL356016.2, AL356265.10, Z84470.1, AC006395.1, AC005018.2, AL445528.16, Z78022.1, AL158819.14, AC026337.29, AL359636.17, AL353897.7, AL365475.1, AL360297.12, AP002026.1, AC090710.16, AL139277.7, AC002429.1, AL355530.6, AC010223.5, AL450338.5, AF128525.2, AL590306.7, AL359925.9, AC026201.3, AL049646.19,</p>

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HDPH151	124	460679	1 - 714	15 - 728	AC005946.1, AC018755.3.
HDPJF37	125	704487	1 - 972	15 - 986	BE262780, BF317450, BF313101, BF207173, AW195799, BE857989, AA311391, AW205695, AI160666, AW262228, AW052051, AA367991, R74203, BF901238, AW026920, R74295, BF880147, AA644389, BE795190, AI934065, BF530635, BF896366, D20643, BC004895.1.
HDPMM88	126	972734	1 - 4879	15 - 4893	AV715713, BF446914, BC057685, BF898163, AI083524, AI290271, AA318526, BF932901, R78174, C17785, R77809, BF898707, AW795715, AI638633, BF921994, BF904690, AW016805, AC025040.7, AK025125.1, AC016045.8.
HDPNC61	127	637585	1 - 1396	15 - 1410	AA847865, AA483400, AI016714, AI051725, N62194, BE047259, BE327006, AA483411, AI554330, AW874660, AA933624, N66755, AI825794, AW327616, AA902896, AA725234, AI769182, BF448730, AA054669, R60056, AA594900, H05474, T16298, AA977118, AI671131, AA054722, AA650410, BE719696, R43427, AA716570, T82929, AW327262, BE044255, AA761969, AW974625, AA916000, T34734, BF817206, AA805766, T90105, AI249880, AA342241, AA811545, AW956711, AA484223, AL354808.24, AC003098.1, AC079602.15, AL049569.13, AC004166.12, AL450325.5, AC005288.1, AC005736.1, AL157838.24, AC027644.9, AP000350.1, AC011475.6, AL022238.1, AC005098.2, AL096791.12, AC006261.1, AL022476.2, AC090944.1, AC008569.6, AC007899.3, AL590763.1, AC020917.4, AC087071.2, AL359397.3, AL135752.6, AC013726.7, Z85986.1, AL354815.10, Z93015.9, AF053356.1, AC002302.1, AC005488.2, AF064861.1, Z83826.12, AL357515.26, AC016637.6, AP001748.1, AL445645.10, AL499628.1, AC020931.5, AC004826.3, AL359091.10, AC004965.2, AL353653.19, AP002852.3, AC020750.3, AC004867.5, AC006001.2,

					AP001705.1, AC005995.3, AC010150.3, AL139289.6, AL031005.1, AL355392.7, AC005077.5, AC006966.3, AC005056.2, AL135901.23, AC009144.5, AP001727.1, AL163279.2, AC009753.5, AC004699.1, Z84466.1, AL157938.22, AC083884.6, AL050341.18, AL355543.13, AC004820.2, U95090.1, AC005844.7, AL353804.22, AL163032.3, AP002812.3, AC005052.2, AL049776.3, AC006117.1, AC007220.4, U95740. 1.
HDPND46	128	637586	1 - 1713	15 - 1727	BG058578, D20888, AL034424. 9.
HDPOE32	129	897276	1 - 1339	15 - 1353	N43024, AA284735, N30921, N33362, AA736727, AA477254, W31624, AL533888, AI350205, AA306490, AL520318, W32089, BE395042, W42796, BE251326, AI951749, AA464683, AI694661, AA298928, AI571803, BE257270, AI021931, AI871631, AL530622, AA071502, C14760, AA622514, AI143235, BE005514, BF216867, AA297690, BE005513, AI023746, AI498301, AW028350, AA477253, BE045131, BF927531, AW024940, AI240266, AI493740, AW295451, AI418206, AI418223, AW779350, BG055383, AI245358, AI911036, AA759227, AA602479, BF215223, AW294426, W89051, AI343854, T62095, AV736738, AI767945, AA977564, AB026899.1, AP000500.1, AC011811.42, AC012507.9, AC006365.3, AC004847.3, AL034376.10, AC005094.1, AL079304.3, AL121857.5, AC025074.5, AC020983.7, AL031407.3, AP002028.1, AL157382.14, AC012512.7, AF063605.1, AL034396.6, BC000642.1, AL163194.5, AC019041.8, AL138720.19, AL356257.14, AC084881.19, AL136374.4, AC008009.4, AL353616.13, AF001548.1, AC078994.3, AL163639.3, AC022002.4, Z84474.1, AP000810.5, AC026421.3, AL162378.16, AL353748.13, AP001694.1, AL136137.15, AC078961.23, AL390316.6, AL024458.1, AC005678.1, AC003012.1, AL139809.16, AP000080.1, AB053170.1, AL049743.10, AL353752.6, U95740.1, AL590074.3, AC003662.2, AC010146.13, AP000086.1, AC019187.3, AL121694.4, AL139382.12, AC005042.1, AC008795.6, AL390027.11, AL133396.2, AP000564.1, AC005510.3, AC024028.10, AC006441.13, AL132985.4, AL080239.11, AL109935.39, AP000964.2, AC073866.16, AC002086.1, AC083867.4, AP001718.1, Z92844.1, AL158819.14, AC005023.1, AC005050.2, AL391867.5, AC007991.7, AP000344.1, AL357752.19, AC005697.1, AL355481.12, AC006452.4, AP001691.1, AC006974.2, AC020987.8, AC004859.2, AC008109.6, AC019205.4, AC010348.4, AC019072.7, AC012067.2, AC004584.1, AL390840.17, AC008270.3, AL390800.4, AC005225.2, AL356052.14, AC004597.1, AL512666. 6.
HDPOH06	130	683371	1 - 2490	15 - 2504	BE790341, BG105222, AV707856, AW955948, AI378660, AA669141, BF725031, AU154522, AI985796, AA688220, AI042515, AI372881, AI014423, AW025175, AI335099, AW263024, AI491990, AW128917, AI570270, AI128127, R91019, W85883, AW474941, N59550, AW305279, BF931700, AA679558, AV653236, AI635705, AI559984, F00878, AW340645, R08677, W85967, AI262108, T98198, AA670170, T53837, BF926938, BE937947, AA337112, AA583164, AW888374, R88760, BF091472, AA902605, BF935752, N78291, BE766705, T98199, AI540509, AK001709.1, AC018648.5, AC003108.1, AC003684.1, Z95152.1, AC010530.7, AC008760.6, AC073101.7, AF334404.1, AC004694.1, AC074121.16, AL391122.9, AC011445.6, AL354815.10, AC010618.7, AC002365.1, AF243527.1, R08585.

HDPOZ56	131	135231 9	1 - 1891	15 - 1905	AI859620, AI830021, AI949469, AI887204, AI218392, AW194364, AW511272, AI307671, AA970014, AW582666, AW609988, AI873619, AC011452, 6.
HDPSP54	132	744440	1 - 3077	15 - 3091	BG256849, BG261011, BG178729, BG110345, AI923220, BE466885, BF667257, AW271504, AW243442, BE466659, BG171469, AV661528, AW271637, AW516811, N36059, AI804888, BE882420, AI650826, BF815232, AW964507, AI921747, BE936373, BF984751, BG259707, AI392784, AW076096, AI807747, AW103424, AA604757, AA633209, AW778887, AW418987, AW242326, BE622192, BF666519, BF978796, AW014203, AI925261, BF853590, AW131363, AW514756, N33223, AI819108, AI126250, AV649748, AI953896, AV714556, AI524472, BF697124, BE218100, AW629098, N21567, AI694687, AI700209, AA731730, AA577191, BE219931, N33824, BE567212, AW778908, AW087660, AI990562, BF792681, R52426, AI559108, AA743389, N35579, N25189, N30972, BF667662, AI339587, N24947, AI376459, AA742979, N27426, R23308, AI125720, AA954281, AI801129, AW087669, AI701246, AI245517, T26975, BF572334, BE177998, BE564497, AI636147, AI640713, N41938, H97662, AI243263, BE967025, AI572028, BE543895, H29641, BE762905, BF246305, Z46022, H29640, BG223352, AI270534, AI983198, H99399, BF965116, BF692452, Z42169, AI521060, BF102948, R82562, AV646807, N34709, AV646406, R23233, AA373475, BE005657, AA319637, T34245, BG104469, W20047, AW962829, BF572695, AI369988, AI741908, BE830524, H29549, D78710, Z41637, H29548, AA833897, AI367191, AA659275, AW899997, F01708, BF697465, AI246035, AI219239, BF154447, AI221561, AI273738, AI281168, BE005723, BE170424, AI685342, BE882847, AB007962, 1.
HDPTD15	133	692917	1 - 1382	15 - 1396	AA428414, AL042853, AA363501, AA723017, AA513999, AI547286, BE072237, BE044986, BG008598, BE153851, AA642060, AA363207, AA828704, C15073, AU147529, AA369477, AW974890, AA483034, AA593060, AI285521, AA558697, AA310158, AW851028, F26152, AA515435, AA828680, F36373, T66105, AA658235, AA551509, AA634227, AW844234, C18357, BF805334, BE958096, BG056233, BG059938, C18360, AA084863, AI133164, BG056088, N43757, BF769505, AA715609, AA419263, AA503947, BF869171, AA653964, AA301813, AW673241, AA450199, AW580735, AA557686, BE153330, AW589633, AI921649, AV709707, AA318652, AI376100, AW955577, AW276435, BF438574, AA021552, BE072020, AW664161, AA715362, BE221335, BF827669, AI453383, AW074059, AI356904, AI564284, BF743037, AW994731, AV759464, N66067, F25593, AI355206, BF769371, AI922654, AA747480, AW575719, AA829106, AA364701, AL041706, BE206021, AW274349, AW953770, AW089789, F36273, H58672, BF940837, AW169136, AI444644, AI372413, AV700545, AV699709, AV700498, AW303196, AW301350, T08638, AU158130, R13151, T96279, AI284640, AA654998, AV700988, AA364193, BE153327, AW249835, AA136829, AA309874, AC020728, 4, AL137787.11, AC068533.7, AP001752.1, AP001053.1, AC004941.2, AC005166.1, AL021579.1, AC008013.8, AL133479.11, AL139022.4, AB016897.1, AL138718.17, AL096712.20, AC037423.16, AC004884.1, AC008733.7, AC007163.3, AL137794.5, AC007312.1, AC078929.27, AC007285.3, AC011533.6, AC009194.8, U95740.1, AL121934.17, AP000144.1, AC006449.19, AC007628.3, AL031591.19, AC027126.4,

				AC011475.6, AC004672.1, AL137068.10, AC007318.4, AL390798.3, AC012076.4, AC008651.7, AL121893.21, AJ295844.1, AL118520.26, AC090937.1, AC004593.1, AJ277546.2, AL139331.19, AP001132.4, AL035681.13, AP001331.1, AC016721.11, AL035413.19, AC009950.6, AL021786.1, AC002429.1, AC007536.9, Z69918.1, AC005625.1, AL161665.5, AL138703.10, AC016831.1, AL031275.1, AP001627.1, AC009516.19, AC006028.3, Z98200.8, AL359400.4, AF029308.1, AP001747.1, AC090514.1, Z86062.1, AC005837.1, AC018797.4, AL109802.6, AB017602.1, AC034305.6, AC005888.1, AC078841.4, AL353597.20, AL031736.16, AC010170.3, AC024571.4, AC005799.1, Z23567.1, AC005225.2, AL109799.6, AL109965.34, AL121928.13, AC024341.9, AC015550.18, AL590106.7, AC010269.5, AC018751.30, AL121890.34, AC068193.7, AL137077.31, AC015651.18, AC004933.1, AC021092.1, AL138706.9, AL137244.28, AC006976.2, AC020663.1, AC008546.6, AL022323.7, AC010235.6, AC006536.2, AC004010.1, AC010489.4, AF064857.1, AC007011.1, AL159977.10, AL160032.14, AC010651.7, AL109804.41, AL031683.2, AC008569.6, AL451049.11, AL391478.14, AC005696.1, AC004453.1, AC024561.4, AC005703.2, AC004905.1, U22376.1, AC004158.1, AC012380.1, AC002400.1, AP001628.1, AL136308.4, AC066612.7, AL139095.15, AL356601.14, AC005215.1, AL356776.21, AC006435.7, AF312032.1, D83737.1, AC009068.10, AC009319.19, AC010134.4, AC005792.1, AC022007.3, AP000252.1, AP001717.1, AP000553.1, M87918.1, AC090042.1, AC005052.2, AL512363.11, AF224669.1, AC002395.1, AC011739.7, AL162503.12, AC073138.3, AF137396.2, AL139328.8, AL356858.19, X77531.1, S78429.1, AP000336.1, AF111168.2, AC004894.1, AC004134.1, AL022476.2, AP000031.1, AC005680.1, AL133548.6, AL049859.7, AL358174.12, AL035608.11, AL161727.15, AC008670.4, AC005736.1, AL121834.20, AC004478.1, AP000215.1, AL513550.9, AC024067.4, AL449363.12, AC026120.33, BC002464.1, AL590420.5, AC011746.6, AL109984.14, AL591004.3, AC020550.4, AL590762.1, AC073325.8, AL390295.10, AC005887.3, AC021016.4, AP000313.1, AC007102.4, AL023693.25, AF108083.1, AL049613.2, AL445201.14, AK022268.1, AL162426.20, AL008629.9, AC090043.1, AL133411.8, AC016617.5, AL391114.12, AL050312.8, AC008277.4, AP000776.4, BF982785, AL815076, AW166997, AL079767, AW151042, BF823103, W63598, BF878473, AA449913, AA976313, AW798524, AA479330, AA846290, BF898435, AA836589, AA630200, AL341675, AL434208, AA157695, AL184716, AL361509, AL216438, AL924429, AL244502, T87329, N26990, BF883126, AL694074, AA157771, AL682580, AA304298, BF883106, AW848681, T87430, AW376555, AW376601, AW376609, AW848666, T64266, AA127194, AA308797, AA854135, T70082, AA974005, T98394, T70152, AL219259, AA304365, AW291861, BF883705, R82980, AA400789, AA449914, AL424501, T98393, AW376580, N40111, BF900907, AL301920, AA442329, AW300876, BE512905, BE902037, BE273884, BE901865, BE166105, R82979, BE311462, BE903644, BE901108, AL284060, BG171620, AL515147, BF811804, AL889208, BE875380, AL628325, BF792951, AL682915, BE906273, AL434233, AL436446, AL362391, BF815930, AL561147, Y18474.2, AJ130718.1, AB011263.1, AK025377.1, AF092032.1, BC003062.1, AB020532.1, AL365451.1, AL365452.1, AL365450.1, AL133448.4, AB031537.1, AB031536.1, AB031535.1, AB031531.1, AB031530.1,
HDPTK41	134	744824	1 - 1550	15 - 1564

HDPUG50	135	684120	1 - 1720	15 - 1734	AB031532.1, AB031533.1, AB031534.1, BC008649.1, AF033827.1, AL133020.1, BC007571.1, AL133074.1, AL136850.1, AL050366.1, AL515943, AL520278, AL531137, AL515942, AL520279, AI217895, AW960744, BF970078, BF001249, BF036496, BE395420, AI983150, BE277851, AW385698, BF979048, BF688139, BE395502, AW374106, AI660124, BF541042, BF210794, BF036241, BE567389, BE778929, BF209890, BF103631, AI339010, AW374124, AA166971, BE564629, BE971080, BE276625, BF509403, AA542906, AA689356, BF695952, AI285269, AI346870, BF541205, BF030313, N27706, BF243030, AW236815, BE567683, AI821227, AI821074, BE566782, AL134542, AA166818, BF570861, BF059406, AA836112, BF695731, D20721, BF130491, BF677074, BG118818, AI221030, AA627350, AW027663, BF106059, N35710, BF674060, BF029128, BE933681, BE933586, AI221246, AW372396, AI285231, T95430, AW372395, AI699709, AL134543, AA055338, AA449417, AW197834, BF030982, R83129, AI418208, AA375954, AA450383, AW958166, AA961046, N20259, AA336834, AA226636, AI911109, AA225691, N20865, AA825421, AI932769, AA938413, AW197872, AA370379, N29162, C03633, AI620095, AA055337, BE694074, AI932771, BF697063, AA976076, BE468082, AI821821, AA173926, AA173884, BE857593, AA569611, AI821883, AA772955, AW383971, AI432644, AI431307, AI431316, AI432666, BE898721, AI431238, AI623302, AI432653, AI431323, AI921241, AI431347, AW968355, AW971740, AI431350, AI432655, AW081103, AI431321, AW968356, AL042853, AL042729, AI431243, AI431230, AI431328, AI432654, AI431310, AI431312, BE672745, AI432650, AI432677, AI431247, BE672644, AI432657, AW972093, AW968729, AI492519, AI431231, AI791349, AI431257, AI431235, AI431354, BE672759, AI431318, AI431353, AI432661, AI431246, AI432649, AI432643, AI432675, BE672719, BE672732, AI431337, AI432651, AI432647, BE672640, AI432674, AI431330, AW972092, BE672622, BE672627, BE672767, BF448552, AW129223, AL045327, BE672748, AW972090, AI431248, BE672742, AL042931, AI432665, BE672626, AW972091, AL042519, BC001133.1, AJ224875.1, AL133082.1, AF064854.1.
HDPUH26	136	866433	1 - 2902	15 - 2916	AL525441, AL525265, AL528202, AW964372, BE747248, BE743063, BF793839, BE005995, BE870109, AV706482, BE645327, AV698161, BE272135, BE254341, AV704424, AV706294, AA772122, BG153419, AA777796, BE645332, AI743322, AV707082, AV706285, BF382272, BF514943, BE018051, BE673957, BE301907, BF114727, AW964371, BF530465, AA897780, AI890748, AI559637, AI688995, AW780354, BE206397, AW137052, N51699, AW103016, BF794314, AA528004, AW662431, AW085759, BF313538, AI765564, AI954974, AI570150, N20494, R87549, F31312, AI245467, AI991886, AA112198, BG170315, BG178458, AW273510, AI435207, AA004881, AW964399, AA005087, N25526, AW608346, F36783, AA587960, AI815015, AA454482, AW662721, AA318288, AW993077, N29111, AI247285, AA911896, AI766414, R91507, AI279757, BF313030, AW242248, AA707000, AI367676, AW139115, T16478, AW504841, W90114, R12114, T32805, AI675726, AA346284, BF765331, AW993187, AA317950, BE169534, BF692514, AW086086, AA186891, BF749263, BG013421, BF765334, R36868, AW769864, AW884956, AI972497, BE170268,

HDPVW68	137	812737	1 - 1734	15 - 1748	C01229, AA348258, AI953592, F27014, AA599852, AI914300, N51791, BF676529, AI868860, T48372, AI824747, F30177, AI810802, AI263284, AW611772, AA188514, AA603987, T32655, AL528203, AI625886, BF874301, AI346660, AA903746, F35605, AW820935, AW577918, AK000303. I.
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HDPVH60	138	796865	1 - 3102	15 - 3116	AA503239, AA005023, BG058640, BF439950, AA494553, AI688402, AI797733, AI436404, AA292931, AW273747, BE675352, AI475570, AA227825, AW062928, AI940630, AI940605, BF356100, AI244665, AI940646, AW374287, AI940639, AI016022, AI348158, AW374286, AI475793, AI222804, AA740395, AI289241, AA731769, AW374280, AA293061, AW176407, AI940666, AI952797, AI863905, AW751215, BE074921, AA347230, AW751228, AI253625, AA722775, BE074922, BE074923, BF091018, AI940657, AA830985, BE246530, AA005022, BE245464, AW194142, BE245946, AW845618, AA679298, AA553743, AW845617, AI986465, AI656229, AI587517, AW845579, AI439199, AI439202, AA905818, AA227999, BF365504, AA347231, AA300784, BF365509, AW062885, AI048537, T61473, AW885247, BG057915, BE247510, AW516362, BF756544, AI762964, AA563914, AI469789, AA903221, BG112718, BG112102, AW411397, AK027414.1, AK027416.1, AK025212.1, AK025362. I.
HDPVW11	139	103699 7	1 - 2325	15 - 2339	AV762219, AL529216, AL529217, AL521330, AL521329, BE277176, BE798017, BE274847, BE868280, BE311800, BE543175, BE410652, AW967107, BE304534, BE900339, BE893443, BE276851, AI679161, AA193416, BE302421, AW474478, BE409098, AW474521, BE349259, AI146528, AI041230, AA614445, BE743095, AI343535, AI400378, BE890338, AA127444, AA458592, AW245738, BE265039, BE281384, AA807821, AI669961, AA317883, BF514665, W48808, AI292224, AI292150, AA902490, AI302370, AI810191, AW245381, AA713501, AI708068, AW975539, AI469722, AA418282, AI192592, AW975538, BE041714, W49817, AA764785, BE742888, N50655, BE389280, N47165, BE241970, AA884873, BE389259, AI826827, AW673387, BF055737, AV746964, BF341801, AW675735, BE886291, BF924882, AL039086, AW403717, AV682124, AL515375, AW806761, AL135025, BE621256, BE047737, AL514929, BG030364, BG027280, BE909009, AA291456, AI364788, N50750, BG249582, AI648663, BE620444, AL036736, AI590120, CI6221, AA508692, BF854113, AW827289, AI922901, AW302988, BF909758, AV729336, BG035511, BG118829, BF343172, BG168696, AI498579, BE538485, BG112879, AL045266, BF970449, AA640779, BE048071, AI829327, AI689420, AI888944, BE965192, BE880190, BG165051, BE905856, BG113299, BF339322, BE874133, BE875407, N80094, AI921248, AV756074, BF828567, BG122481, AL041772, BF968205, AW006046, BE964812, AW071417, AI308032, AI344785, BF696282, I.

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HDPWN93	140	992925	1 - 2665	15 - 2679	AL518824, AL518825, AL528951, AL528952, BF339524, BE546359, BF966792, BE736522, BE737435, BE883235, BG109398, BE314676, BE787143, AL534022, BF446115, BE894833, BE870112, BE881800, BE258349, BG250236, BF196311, BE894832, AW769380, BE262368, BE882948, BE259378, BG251409, AA432202, AI890824, AI753494, AI651671, AA993211, BE246045, AW001898, AL039524, AI800905, AI246773, AI682295, AI658613, BE273831, AI631136, AW189302, AI372827, AI050708, AA531521, AI346388, AI683842, AW296359, AW372955, AI685246, AI589722, AW271749, AW804759, BE548044, AA622365, AI552313, BF906035, BE163138, AI088281, AI372826, BF109450, AI05389, AI539826, AA349564, AA448189, AI760986, BE882927, BE247210, HI15544, HI15545, AA349563, BF924519, BE245469, AW804423, H09846, AI991731, AA320029, AA383782, BF804839, HI15604, W67789, HI15603, AI015277, R33930, BF869179, AA543091, AI469944, R48594, BE301391, H09761, AA830547, AA505499, BF809086, AA320560, BE273649, AA326027, R79459, AA322654, L32015, C20992, AI828309, AW117647, BF000032, AW190887, BF736822, AW262975, AA317254, AA143736, BF381075, AW103622, AW050451, AI609346, BE720302, N21451, AI905534, AA282625, AW007401, AA284991, AA621245, BF841809, BE146295, AA143707, AI811818, BF326108, AA393671, BE242665, BF746024, AI678229, BF799280, AA429592, AW407359, BE075823, AK025000.1, AK025622.1, AC004590.1, AF086245.1, AP001434.1, AP000161.1, AP000020.2, AP001731.1, AL137367.1.
HDPWU34	141	630354	1 - 1263	15 - 1277	BG054851, BF439942, AI141684, BG008949, BE677186, AA242853, AI281834, BF433831, N50984, AA826047, AW014432, AA977801, AW770255, AA984041, T64272, AA994205, AA252172, T64144, AI361098, BE146421, AW084330, AI280735, AA931748, AW071613, R09320, AA448980, AI990634, R09211, AW388104, AI147841, AI198101, AW517751, AW238793, BF969846, AI627898, AU156992, AW074546, AW072130, AI276023, AI457707, AI394689, AI953242, AI539262, BE907440, BF984530, AI886594, AA761557, AW082532, AI613471, AA947158, AI380329, AW079334, AI636788, D44958, AI568132, AI274769, AA150147, AI624304, BF828567, AI933785, AW248417, AL036548, AI934147, AI343038, AW302662, AI336506, AI254251, AW303238, BF054886, AW268290, AI318301,

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HDQHD03	142	130917 5	1 - 1252	15 - 1266	AA769067, AA907349, BE676751, AA804234, AA906120, AA830952, AA743729, AA835876, BF434668, BF838119, BE837591, BE837571, BE827732, AA318133, BF807079.
HD7BD53	143	972757	1 - 2789	15 - 2803	AL521719, AL039239, AL522288, AL521718, AW850549, BE745185, BG036401, BF971064, BF982318, AV752274, BE410288, BF970662, BE179100, AA115485, BF037889, AI903708, W74580, AV752030, BF207332, AW069193, AW850706, BE260313, AA114996, AI147007, AA287865, BE294206, AA779902, AW953654, BF203424, AA287665, BF102950, AW089856, BE081349, AI424273, AI337872, W75992, AA039973, AW615357, AA287868, AA040007, AW207183, AW630077, AA844006, AI092051, AA035003, AW374784, W79563, AI095505, AI370765, C05140, AI961895, W92237, BF056098, AI431633, AA011411, AI381447, AA922367, AA688312, AI860011, AI200662, AA676566, H08173, AW590492, BG222429, AI741707, C02948, AA609401, AA427979, AV739012, H29396, AA453991, BE894938, H01836, BG165095, BF333733, W70295, BE242586, N41910, AA054984, R24822, AA156412, BG055899, H48740, H08272, AI241860, BE763810, T63735, R34728, Z42796, BE936536, W88710, AA367891, R36564, Z45070, AA412324, R78131, R56319, AA709055, AA429366, AI915050, AW673132, AL522287, R14984, AA347579, AW023366, AA853400, AA853401, W52589, AA476640, T39346, W88711, AI282590, T29951, AA411419, AA360166, T80320, AA331893, AI754899, AA602993, AA506382, R01609, AA328290, BF808365, N56432, AI832140, AW890834, T31756, R45735, BE929124, AA887981, W31306, BE710919, BE169167, AA039914, BF748450, AW381600, BF352203, AA648132, AI564214, R36407, AW374826, AA383447, T53688, AW198043, AA368172, T53689, N92423, BF237454, AA304402, D79323.

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HDTBP04	144	130774 2	1 - 947	15 - 961	AB055290.1, AB049892.1, BC005073.1, BC008364.1, AK000137.1, BC004899.1, AL133640.1, BC000677.1, BC007456.1, AB048954.1, AF218033.1, AB048974.1, AF113222.1, AK025350.1, BC003682.1, BC004310.1, BC002342.1, BC002736.1, AL137656.1, AL133619.1, M80340.1, AK024546.1, BC004368.1, BC007499.1, BC004960.1, AK026865.1, BC008185.1, BC009221.1, AJ001838.1, AK026504.1, AF069506.1, AL080154.1, BC007657.1, BC006410.1, AK026630.1, BC008784.1, AB060917.1, AB055368.1, AF262032.1, AL133062.1, AF260566.1, BC001336.1, BC004119.1, AL050143.1, AF081571.1, AL136586.1, AL080148.1, AF000145.1, AB062750.1, AF227198.1, AL133665.1, BC009294.1, BC002733.1, BC000253.1, AK025383.1, AK026592.1, AK000418.1, BC002809.1, BC001790.1, AK026155.1, AL353957.1, AB047930.1, AK027204.1, BC001964.1, AB048975.1, AB060852. 1.
HDTDQ23	145	130698 4	1 - 2193	15 - 2207	AI872206, BF966561, AW513884, AI912340, BE856991, AI758821, AW337178, BE327923, AW004890, AI572080, BG109128, AW058001, BF342854, AW886887, BF967940, AW474823, BF337371, BF591084, AA775261, BG164538, AA831357, BE087219, AW074361, AI361820, BF696525, AI982775, BF793075, AI690445, AA581345, AU156793, AI917776, D20022, AA825538, BF382552, AI360561, AW439592, AI798286, AI140796, AI277190, AA100279, AA485257, AA835492, AI522238, AW517943, BG035022, AI015234, AA706811, AI469550, BF197859, AI689240, AW265061, AI744762, AW450726, AI884872, BE714642, BE138867, T34498, BF213985, AW769512, BE073192, AA122332, BE138831, BF090537, AI811224, BG167993, BE932894, BF980823, AI355770, AA092467, AI471817, BE904497, BE719958, AI702026, BE171537, BG166879, AI597962, BG180321, BE171499, BF914841, BF967213, BE932875, AI681670, AA089786, BE327680, BE219939, BF032916, AU136610, AI624976, AK001917.1, AF035606.1, U58773. 1.
HDTEK44	146	102542 1	1 - 2056	15 - 2070	AW263031, BF939317, AU158582, BE326883, AI825947, AI674408, AI949058, AI686114, AW236450, AI131456, AI921750, BE646223, AI499386, BF241709, AI744116, H17702, AA968971, BF197318, AI202380, AI612728, AW151821, AA612626, BG010826, AI568798, AI678940, AI868979, BF748934, AW084407, BE075305, AK023814. 1.
HDTEN81	147	571078	1 - 552	15 - 566	AI718421, AI431290, AI332560, AI391465, AI638172, AA507382, AI734920, AA719940, N70479, AI253742, BG059093, AI708198, AI510752, AI637680, AA505271, AI719838, AI707589, AA614722, AI862746, AI830189, AW269501, BE041192, AI471305, AW512571, AW518210, AI708443, AI749344, BG236645, BG059064, AW268642, AI468901, BG059125, BG231197, BG151405, AW877209, AI119457, Z99396, AI119324, AW973213, AW975037, AW973219, AW975954, AW969816, AW975027, BF686897, AW972845, AW861944, AW975002, AW971975, AW974998, AW804686, AW975154, BE705905, AW973230, AW979127, AI119399, AW969680, BF868687, AW969885, AW975692, AW392670, AW979098, AW972292, AW604723, AW975965, AW974801, AW975876, AW979106, AW976031, AW976024, AW975632, AW975032, AW975971, BG153750, AW975966, AW975019, AW975930, AW979090, AW975105, AW975981, BG151745, AW969673, AI718421, AI431290, AI332560, AI391465, AI638172, AA507382, AI734920, AA719940, N70479, AI253742, BG059093, AI708198, AI510752, AI637680, AA505271, AI719838, AI707589, AA614722, AI862746, AI830189, AW269501, BE041192, AI471305, AW512571, AW518210, AI708443, AI749344, BG236645, BG059064, AW268642, AI468901, BG059125, BG231197, BG151405, AW877209, AI119457, Z99396, AI119324, AW973213, AW975037, AW973219, AW975954, AW969816, AW975027, BF686897, AW972845, AW861944, AW975002, AW971975, AW974998, AW804686, AW975154, BE705905, AW973230, AW979127, AI119399, AW969680, BF868687, AW969885, AW975692, AW392670, AW979098, AW972292, AW604723, AW975965, AW974801, AW975876, AW979106, AW976031, AW976024, AW975632, AW975032, AW975971, BG153750, AW975966, AW975019, AW975930, AW979090, AW975105, AW975981, BG151745, AW969673.

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HDTFE17	148	104339 1	1 - 1228	15 - 1242	BE273962, AW675159, AA621888, AA621871, AW748710, BE151868, BE151889, BE151869, BE151849, BE151872, BE151870, BE151871, BE151873, BE151864, BE151839, BE151843, BE151866, BE151846, BE151874, BE151850, BE151861, BE151882, BE151862, BE151890, BE151845, BE151844, BE151885, BE151854, BE151841, AW748711, BE151847, BE151865, BE151886, BE151969, BE151887, AW748719, BE151842, BE151883, BE151963, BF350425, BE151880, BE151851, BE151968, AW748716, BE151904, BE151853, BF350436, BE151840, BE151905, BE151907, BE151884, AW748723, BE151901, BE151974, BE151966, BE151964, BE151848, BE151912, BE151897, BE151888, BE151902, BE151896, T56553, BF350423, BF350431, BF378245, BF350424, BE151979, BE151987, BE151913, BE151908, BE151911, BF350422, BF350432, BE151852, BF350429, BE151900, BE151970, AW374334, BF350430, BE151899, BE151881, BF350438, BE151973, BE151914, AW087213, T08905, A1652677, A1673648, AW246689, BE151978, BF355903, A1655004, AW250829, AW672991, BE151962, BE151977, BE151967, AW170222, A1140471, BE151910, R94667, A149673, AW183216, BF345144, BE151976, AW189831, BE151975, AA612723, BE151903, BF350418, AA149754, BF312447, AL517947, AF276889.1, AF196972.1, AL136967.5, D82352.1, W35383, AA015734, AA015831, AA018179, AA020824, AA020847, AA021564, AA021617, AA088190, AA088363, AA261917, AA262421, AA418866, AA426526, AA430530, AA613360, AA573487, AA577277, AA761384, AA831386.

HDTGC73	149	635457	1 - 698	15 - 712	<p>AA864866, AA902924, AA922543, AA934011, AJ052766, AA481843, AA481990, AA433981, AA844171, AJ004425, AJ033046, AJ073848, AJ087207, AJ088106, AJ093860, Z38440, Z42185, AA683532, AJ272861, AJ285507, AJ301768, AJ343925, AJ351185, AJ356409, AJ359625, AJ479005, AJ569081, AJ582503, AJ147150, AJ623660, AJ184904, AJ193793, AJ264308, AJ273503, AJ587448, AJ351022, AJ632302, AJ621103, AJ670930, AJ698414, AJ701275, AJ801704, AJ868864, AJ888089, AJ916106, AJ949047, AJ963403, AJ970843, AJ989788, AW073000, AW132028, AW196624, AW207687, AW193329, AW511737, AW590114, AW590183.</p> <p>AW022607, AW511178, AJ140427, AJ971228, AJ373655, AJ580779, AJ369886, AJ190934, H40803, AJ243231, AA453827, AA453746, BF446909, BE326968, AA961079, AA040716, N47998, AJ819706, T56239, H39994, BE670797, AJ749775, T56381, H43297, BE464767, AA988630, AA974652, AA442300, BE327694, C01257, R49917, F34030, R17933, AA987718, AW440024, AJ018768, BF942310, BF446776, AJ240357, AJ400446, N24874, N78913, AJ694117, AJ002282, R49918, AJ685705, BF942188, BF942316, AJ972263, AA437235, AJ498099, H39563, BF964549, H43296, T47759, AW900854, AA968952, BE887988, N51205, T47760, AW779345, AA040717, AJ873997, R18029, AA933016, BF885380, AJ687282, AL096888. 30.</p>
HDTIT10	150	839264	1 - 1186	15 - 1200	<p>AJ083677, BE743996, BE743947, AJ160678, AW664068, BE349558, AW628596, AJ571248, BE855557, AJ074410, AJ187067, AJ570161, AJ369658, AJ911489, AA847560, AJ858954, BF061712, AJ633548, AJ797227, AW131565, AA740410, AJ523334, AJ016601, AJ381898, AA456612, AA044598, AA059399, AJ459164, AJ090345, N35134, BG222539, AW167314, AW573046, AW189552, AA909759, AA937341, AA507905, AA029634, AA402030, AA857843, H50249, AJ040383, AJ457950, AJ017968, H49423, AA761742, BF056436, AA454713, H41354, R53884, AJ808070, AA983678, AA402973, AA757454, R89047, AA814131, H46258, AA503217, AA621290, AA484401, BF447031, R67742, AA805632, AW163079, R50125, R82044, AJ948622, AA484466, AJ356460, AJ095617, AJ910985, BF510966, H27862, H43711, AA935660, AA604173, BE139470, AA868478, AJ468101, AA317664, AA554872, AJ582858, R90731, H51590, AJ243984, H43799, AJ399885, AV697638, AA662796, AJ417135, R53883, AJ400568, AJ298084, AJ216579, AJ399848, AA973892, AA455791, AJ937339, AJ147045, AJ132122, AJ809110, AJ132019, AJ824141, W69465, N32856, W73351, AA993580, AW518179, AJ026644, AA828309, AJ934497, AA622497, AA524758, BG152377, AA029064, AJ571725, AV695520, AA029168, H41046, BE844032, AJ566678, AA863413, N41809, W73471, AV697639, AJ245117, AJ524611, BE041443, AA877127, AA876431, R07464, AW303296, AA761499, N58964, Z19469, H41261, AW193802, AJ972555, R00241, R66131, R87416, BE798222, BE790927, AV744175, AJ168456, AJ025988, BE799623, BE790659, AJ362716, AA805362, F00403, AJ498734, AJ088547, BE790553, AA988398, BE792056, BE903078, BE734036, BF003146, BF953534, BE795218, AA401590, AA058850, AA400077, AA454762, AJ568737, D45613, BF183343, F22545, BF317353, BE793747, AA620552, R07463, BE902702, BF316315, BG104176, BG104243, AJ889953, AJ857296, AJ468872, AJ829327, AW073994, AJ953866, AJ520809, BG256090, AW190042, AW073697, AJ538085, AJ500077, AJ628217, AJ439745, AW198075, AL040243,</p>

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HDTMK50	151	101148 5	1 - 1338	15 - 1352		AI862716, AV740009, BF681619, BF814446, AW955693, AI004591, AI754653, BF941382, AI040051, AW438542, BF984807, AW029515, AA582554, BE393367, AA579179, AA720732, AI733856, AU152964, AA584489, AA528390, AA602557, AL038936, BE019467, AW328331, AV721886, AV726332, BG222269, AW500029, BE294700, AW188662, AI037897, AA171941, AA503298, AI733037, AA535216, BF725844, AI366902, BE676915, AW575605, AL040054, AU152561, AA410788, AW976010, AW512196, AA584148, AI921765, AV764259, AI809818, AW970970, AV685117, AW515437, BF934301, AA121777, AW402458, AA804726, AI566408, AA812684, AW271904, AU118200, AI601229, AU156313, AI689198, BE156426, AV701116, BG222875, AV687683, AV685479, AI818332, AW963444, AI653776, AI292236, AV651051, AW407578, BF871476, AA644090, AW900516, AI628219, AU147341, AI963856, H79633, BE674952, R91911, AF312915.1, AL157838.24, AL161626.20, AP000247.1, AC005726.1, AC073073.2, AC007207.22, AL022324.1, AL353668.18, AL161626.20, AP000247.1, AL359091.10, AL162377.10, AP000115.1, AC006312.8, AL445685.17, AC004212.1, AP000047.1, AL359091.10, AL050335.32, AC002544.1, AC002301.1, AC005332.1, AL357515.26, AC003029.2, AL162272.10, AL050335.32, AC004847.3, AC009331.5, AL030996.1, AC010489.4, AL132713.11, AL139100.9, AC020983.7, AC004847.3, AC009331.5, AL030996.1, AC010489.4, AC008771.4, AC004491.1, AP000925.5, AC005041.2, Z82206.1, AC007097.4, AL133163.2, AL022323.7, AC002039.1, AC004832.3, AL157369.7, AL161775.20, AL161421.11, AC006539.1, AL359839.4, AL157823.9, AL450325.5, AC024028.10, AC034193.4, AC012170.6, AP001711.1, AL358334.3, AC018808.4, AL035530.11, AC005043.2, AC022116.5, AL391868.15, AP000504.1, Z93241.11, AP001710.1, AC004859.2, AL161779.32, AL162505.20, AL445222.9, AC006165.1, AC007022.2, AL133500.3, AC011484.4, AC027319.5, AC005399.19, AC006435.7, U91326.1, AL390294.19, AC002073.1, AF003626.1, AC020552.4, AL138976.5, AP001725.1, AL022313.1, AC005518.2, AL138880.14, AC005057.2, AC018828.3, AC004019.20, AC021036.5, AC010320.9, AF129756.1, AC022383.3, AL034405.16, AL121905.23, AL021155.1, AC007956.5, AL590762.1, AC006511.5, AC002306.1, AL139809.16, AL354808.24, AB023051.1, AL135928.6, AC002476.1, AC005519.3, AC004590.1, AC012384.16, AC005620.1, AC006581.16, AL096819.17, AP001873.3, AP000208.1, AP000130.1, AL138741.13, AL078581.11, AC009086.5, AL109806.22, AL079335.29, AL117382.28, AL022100.13, Z84480.1, AF001549.1, AL590763.1, AC073520.6, AC004707.1, AP001717.1, AF312032.1, AC002045.1, AL139095.15, AL133411.8, AC007050.25, AL355803.15, U82671.3, AL360227.17, AC004687.1, AL021546.1, AC008755.6, AC011311.11, AC009312.4, AC008747.5, AL022721.1, AF196779.1, AL139322.13, AC020898.5, AC008379.6, Z69653.1, AL121972.17, AC011480.3, AC005013.1, AP000512.1, AC011487.5, AC010359.5, AC011895.4,

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HE2DY70	152	722217	1 - 625	15 - 639	<p> AI983739, AI093491, BE464707, AA169811, AA232650, AA609946, AW023590, AW163464, BG260037, AW087445, AL515047, BE785868, BF680131, BE045182, BG257535, AI344817, AV712673, AW071417, BG179993, BG110517, AI345746, AI251205, AA830821, AV725055, BF726237, BF342070, BF792961, AI308032, BF344652, AL514129, AV711509, AV715560, AI802542, BE964614, AL079963, BG163618, BF726183, AI969641, BF970731, BG164371, BE910703, BF037097, BG104782, AW827289, AW103371, AL120853, AL110306, BF885081, AI929108, BE964876, AI815855, BF904180, BF856052, BE965432, BF792469, AI340603, AL514529, AL514357, BG035511, AI521012, AL036802, AI344785, AV681719, AI590120, BE966443, AW935969, BF793309, AV682051, BE047852, BE620084, AI620517, BF341801, BF969494, AA225339, AI909666, AL043981, AL037454, BG109221, BG109270, BE874133, BG110684, BG120816, BF904258, AA427700, BE018334, AV654624, AV764282, BE965014, BG036846, BE048071, AI364788, BE789764, AI619502, BE964497, BF816811, AV706744, BF970768, AV703585, AL119863, BF526407, BF037484, AV660662, AI537677, BG168549, AW082594, BG180996, AI627880, AI471361, AV764180, AL080046, AI569583, AI400725, AW999049, BG261093, BF526020, BG121222, BF133418, AW026882, AI866741, AI536685, BF527014, BF812938, AL036804, AV682289, AI623682, AW268220, AV714485, BE964593, AI349645, BE905394, BE619280, AI433976, AL119791, AV686346, AI497733, AI433157, BE964460, AI619716, AW167222, AI702073, BF910810, BG180046, AV764059, BF812961, BF812960, AA640779, BF344691, AW978080, BG179633, AI348897, AL045500, AI699865, AA572758, BE964636, BG114104, BF921291, AW075305, AI612913, AL041772, AL513943, BE965621, AI340519, BG058398, AI921248, BE965481, BE904902, BE891101, AL121270, AI922901, AI282326, BF904265, BG249582, BG252914, BG105099, BF885675, AI783504, AA814407, BE879906, AI620284, AV681647, AI358701, BE965067, BG168185, AW087901, AW238730, BG168696, AV733470. </p>

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HE2EB74	153	513662	1 - 1420	15 - 1434	AL133104.1, AK027114.1, AL049938.1, AB048964.1, AL050024.1, AK025484.1, AF177336.1, AF210052.1, AL136843.1, AK025573.1, AL157482.1, AL136845.1, AK000718.1, BC005678.1, AL137476.1, AL122123.1, AB055366.1, X82434.1, AL049300.1, AL137550.1, AK026642.1, AK000137.1, AK026885.1, AL133568.1, AL117394.1, BC006195.1, AB048974.1, AK027200.1, AF125948.1, AF162270.1, AF271350.1, X72889.1, AK026464.1, AK026353.1, AF132676.1, AK026542.1, AF061836.1, AK000212.1, AL512719.1, AB063079.1.
HE2EN04	154	545008	1 - 356	15 - 370	BF431622, AL035942, AW500190, AW889139, AA136080, AW304923, AL035941, AA491000, AW002842, AA992811, AA747222, AW189910, AW026264, AA679646, AA953459, BF910533, BG179993, AW162118, BE408392, AA505898, AV682249, BF982063, AL049442.1, AL122116.1, AK025435.1, AL110223.1.
HE2FV03	155	396139	1 - 2053	15 - 2067	AW001928, AW079751, AW073814, AT754638, BG250988, AI884973, AI571035, AW440401, AW082774, AI888810, AW166812, AI250234, AA292765, AA883763, AA706968, AI375629, AW470061, AI367655, AI816708, AA866114, AA706948, N66757, AW103401, AI023713, H99221, AA143778, AA969210, W90744, AA877946, AI289492, AI446437, AI520961, AA604695, AW409669, AW770358, BF220234, AV660129, AA573448, BF698763, AA564001, BC000411.1, AF067656.1.
HE2NV57	156	740750	1 - 853	15 - 867	AL043591, AV726971, AA127856, BE503097, AI879075, AA917899, AI240219, AW958109, AW958106, BE221298, AI761889, AI042518, AW160850, AT750090, W38699, AW157481, AW161163, AA132116, AI565447, AW151293, BE890471, N94930, AI922328, BF476776, AI650737, BF668030, AA030052, AA907159, AW163661, AA127886, R26504, AW160606, R26476, Z33583, AA483553, AA922649, AA974552, AA029940, Z39533, AI700171, AA450258, AW472819, BF445592, AI572746, T30697, T31442, AA568420, AV748357, N55856, AA095728, AW952127, T36214, H89692, F04756, Z44852, C16580, AI873861, N71935, R40796, D62931, AA091396, F06009, F06010, BF927136, AA579325, AW663027, N56262, H89758, AL161449.7, AJ001319.1, AF093419.1.
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HE2PD49	157	638617	1 - 1408	15 - 1422	AC009498.3, AP001699.1, AL138976.5, AC008064.2, AL357507.9, AP001670.1, AL137061. 12. AI143226, BF792579, BE798123, BG027947, BF512811, AW960702, AA074614, AW973179, BF793801, BF970034, AI816250, AI336874, AI359462, BF196595, AI920941, BF683421, AW404001, AA041535, AI619673, AW080448, AA312966, AI248170, AA552215, AI864909, AI161255, AW027101, BE393360, AA613058, AA953791, R54079, R60168, AA426568, AI697713, BF208847, AA082536, AI269146, AA989378, H21497, AA877154, H98486, AI206064, BE563486, AI582707, AI587399, BF677141, BE396204, AI144140, AA527643, AI282213, BE832689, AW574900, AA376459, H29536, AI200580, AA329522, AW662882, BF213405, AI927727, AA318044, AI263946, AA039912, AI223111, AI912507, AI829375, R49273, BF842875, AA091789, F36491, N40052, R39339, AI557366, T24757, R43134, AA425093, AA873687, AI816330, AI266123, AW361339, R60167, AW996248, AI872739, AI561274, BE714945, BE714961, N31309, F31801, R17888, BF904855, H29628, BG119615, D26032, C00043, N27118, AI005232, AI052315, AA301581, N22922, H39166, BC004878.1, AF353991. 1.
HE2PY40	158	753229	1 - 1274	15 - 1288	AA330504, AC000397.1, AF100978.1, X84749.1, AF170890.1, AF100973.1, AF100970.1, AF100962.1, J05175.1, AF134415.1, AF134412.1, AF134413.1, AF134414.1, AF021846.1, AF071831.1, AF134416. 1.
HE6EU50	159	411998	1 - 1138	15 - 1152	AA702142, AI078434, AA069425, R10241, W86987, AI902844, R10745, R10723, AA069424, AI902901.
HE8DS15	160	847060	1 - 2185	15 - 2199	AV725650, BE161426, AW130367, BF434057, AA127680, BF575221, AI096437, BF941499, W58383, AI161240, N95226, AW966449, AI356752, AI093508, AI057144, AA044288, AW130361, AI423547, AI221152, AI094774, H47283, AI352542, AI891136, AI002491, T53270, AA044116, R48378, R24320, AV658066, AI829703, AI819388, BE140169, Z44849, R16574, T39273, AA095159, Z25099, AW273857, R16633, AA384077, AI245095, AW026140, T93764, BE927909, N73937, AW118768, AA121543, AA995178, AI453845, AA703455, AI452494, AW044037, H40993, R48277, AW629019, T64039, AA904647, AW073189, W21055, AW263913, AI096938, Z28777, W03697, AW797518, AI039546, AI434419, AW050649, BG003285, AI240412, AA886341, H23905, AI695284, AI767991, H47284, AI309041, BE927916, AA724059, AI352281, AI584012, AA618131, AA357401, AI796309, BE936061, AB018301.1, AL096772. 5.
HE8MH91	161	589450	1 - 1747	15 - 1761	BF969305, BF059262, BF434869, AI761909, AW137210, AI283077, AI625814, AA910871, BF028374, AU145480, AW103833, AW978231, AA179892, BG111607, AI751270, AU157325, BF970781, AA169699, AI818898, AA169226, AA180424, AA744012, AA806038, AU153225, BF445787, AA630387, AI185702, AU119050, R69144, AA282527, R69260, AA332623, AI625888, AA282635, AA968997, AA744320, AA044588, AW513757, AA196702, BE089435, BF154666, AA248976, AA720672, AK023183.1, AK000289.1, AB055279.1, AK002033. 1.
HE8QV67	162	105007 6	1 - 1985	15 - 1999	BG119583, BE746475, BE745466, BF309488, AI361796, BG170779, BF966754, AW958421, BE617929, BG113523, BE394923, BE858188, BE731439, AA535135, AA236263, AW958336, AV752251, BE222593, BE797087, AI378612, AI634494, AA742437, AI199786, AV752842, AI669796.

					AW571509, AA063366, AI291989, AW004941, BE208151, AV704111, AI871167, AI540336, AA641240, AI288465, AA995997, AI218558, AW803217, AI083642, BF310733, AI435447, AW000866, BF934819, AV702400, N58967, AA136332, AA401608, BF433811, BE044647, AA868416, AW249910, AW627730, AA070405, BE908878, AA805715, BE717281, AA731211, AA844218, BE829627, AA725610, AA401477, BE829527, AI299157, AA648375, AA670304, AA709453, AA283820, AA970204, AW771046, AW249690, AA235005, AI928576, BE829555, BE829559, AW780342, AI017819, BE829626, H72154, AI750471, BE767520, AI571553, AI493322, R49561, AA875884, T70282, AA621993, T92727, AW469575, AI081826, AW449174, AI917238, N99124, BE836842, AA354609, W81566, AI033218, AI357261, AW104863, AV707204, AI445295, W81613, AI983491, BE717246, T08002, AA890368, AV707554, T03334, BE717260, BE836791, H72067, AI359915, BE836784, AW166060, BF834444, AA393274, BE836790, AW949521, AA736679, AA760993, AI085191, AW079503, T91829, AA136418, AA844211, AA725212, AA398623, H72162, BF590157, BE717249, BE717270, AA309678, BE829551, AI301810, BE717253, BE717247, AI500601, BE829537, W96196, AI200943, BF343587, T81071, N57909, AI419052, AI672790, H43667, BE829547, AA721731, AV708653, AI581665, AI208088, R60516, T35798, AW997309, T09191, T92806, BE717235, BE717244, H44738, R44088, AV685266, R30891, AA223393, BE791873, T32074, AW958289, BE000527, BF002298, AW080583, R30822, D80992, AI453195, AI937049, AI004756, AA446567, AI077535, AI291831, AA490386, AW581226, T16726, AI445223, AW074198, T81236, BE702357, AA988970, FI3762, T32218, AA932644, BE717232, AA096082, AI351030, BE762886, AI611828, W96071, AA330722, BE908528, BF084648, BE699273, AA428987, BE019772, AW151622, AI400847, AI799907, BE646085, R37736, AI597679, T34475, AI885091, BE966358, BE717241, BE699278, AA707288, AW580306, T81023, AI825339, AV698582, BE164999, R13905, AA429119, AI160361, T08003, BE829526, BE829579, BE793734, AI133410.31, AB046825.1, AK027884.1, AF258662.1, AF211847.1, U59629.1, AF211848.1, AF009368. 1.
HE9BK23	163	675382	1 - 1622	15 - 1636	AW299658, AV659209, AW058550, AI796131, AW299514, AV658836, AV653227, AV654722, AV682016, AI767984, AV647576, AV649623, AW614624, AI634858, AW235128, AI498692, AV649245, AV693284, AV659141, AI373251, AV653105, AV658636, AV688654, AI796532, AV657125, R86161, AV647536, AV647454, AV660968, AV654145, AV684193, AV659149, BE971322, AW295829, T73510, T73442, AV699707, AV685476, BF740041, N71226, AV726104, C15737, AV706064, AV706545, AV702961, AW962458, AV703159, AF152562. 1.
HE9CP41	164	560625	1 - 1378	15 - 1392	BF032830, AI121944.14, AI138700.18, AI132988.4, AI138805.8, AC018695.6, AC005305.1, AC015853.8, AI049637.43, AC005536. 2.
HE9DG49	165	129993 5	1 - 703	15 - 717	BF508798, AI829099, N25625, AI126506, AI200037, AI128843, AW024969, N34223, AW450603, AA743134, N36303, AW020616, AI217597, AA605122, AI160533, AA729493, AA568193, BE857354, AA568681, AI695490, BE855663, BG054946, N26904, N24885, W52651, AI802647, AI312534, AA648514, N72137, N35103, AA806507, AA729125, N34254, AI219599, H86995, N39790, R73200, N26781, AI032141, N25653, H86994, W00385, R73137, AW298649, AA296449, N28403, R26304,

HE9HY07	166	420063	1 - 818	15 - 832	AW452862, AW453038, AI299683, AA988539, AI141901, W52017, AI039557, AW236299, AW515490, AI361669, AI674252, AA768761, AI452444, AW629545, AI984739, AW074182, AW583163, T25829, AI805445, N20053, BF958127, BF964329, AA543074, BE081422, T25828, AA58828, BE152130, AA653691, AI362330, AW606102, BE170656, AF238079. 1.
HE9NN84	167	846309	1 - 720	15 - 734	AA595746, AI675996, AA421107, BE467349, BF591596, AI760653, AI676145, AI937171, AL048289, AA142958, AV757675, AA211421, N20332, AI048288, AA211732, AI168158, AA150469, BF439049, R70617, AA114851, N20324, AW971316, AA525099, AA527928, AI022578, R49331, AA114852, AI879609, AI350105, AW271678, AA397997, AA400333, AA449237, H10050, AA987243, AA400158, AI632706, Z19420, F00068, H97392, D54580, AI273157, BE220088, BF195338, AW297795, R49240, BF672343, BE327708, AA903792, BE833437, BF681090, BE467754, AW022151, C16456, D55902, F00315, R39349, AI500072, AI919009, Z25269, C01892, N27598, BG026508, D51002, R70518, BF195496, H00776, AF070533.1, AF283527. 1.
HE9OW20	168	135233 7	1 - 1195	15 - 1209	BE738133, AA223584, AU152161, AW297936, BE242781, AU130144, H54044, BE154665, AJ312278.1, AC046130.25, AK027657.1, AK023061. 1.
HE9RM63	169	886167	1 - 2135	15 - 2149	AU133294, AI057619, AI815558, BF949735, AW272417, AI631144, AI083492, BF696663, N53095, AI922624, AI016358, AI791895, AW439093, AA377170, AW238991, AV733682, AI634595, AI280306, AA326937, AI816503, AK001735.1, AF227906.2, AL162500.15, AL158192.15, AL133051.1.
HEAAR07	170	561524	1 - 1070	15 - 1084	BF035327, AI436352, AW903499, BF839884, AV731158, U49973.1, AL136168.4, AC018719.4, AC010386.5, AC026463.4, AL356859.12, AC025097.41, AC010485.5, AC006343.2, AF222856.1, AF222854.1, AF042484.1, AF222855.1, AC005728.1, AC012081.16, AF241734.1, AL158201.19, AC022392.4, AL118557.5, AF002500.4, AL031671.12, Z82975.1, AL139182.24, AP001533.4, AC005317.1, Z98745.1, AC079319.19, AC005411.1, AC004941.2, AL445204.3, AC006566.2, AC005678.1, AL357394.11, AL356094.11, AL356534.12, AL359703.13, AP000893. 5.
HEBAE88	171	526417	1 - 568	15 - 582	AI732427, BF445282, AA129395, AW880236, AA065052, AC004478.1, AC004388.1, AC010722.2, AC007511.8, AL450333.13, Y08991. 1.
HEBBN36	172	486120	1 - 1032	15 - 1046	AW965787, AA426185, BE669482, BE504215, AI823764, AA400753, AW183532, AA099541, AW994875, BF131705, AA676425, AW450178, BE835748, AA693746, AI168628, R26928, BF331783, AA356625, BG150194, AA954744, AA903008, R26705, BE138808, BE019804, AC005180. 2.
HEBCM63	173	484643	1 - 544	15 - 558	AW138816, AI907676, AI360241, AW341219, AI360299, BF477880, AL119663, BF928245, Z38680, AI937380, AI557264, AA170832, AV741220, AV745417, AI524890, C15120, C15762, D52835, AV705545, AI525431, D53447, AI541374, D53472, AV746010, AW965902, AW954735, AV684168, AV726916, AI546891, AV661866, AV702189, AI525306, AV707931, D61254, AI541307, AB023144.2, AL050253.1, AB041736.1, AL023513.1, AL035545.1, AL078460. 6.
HEBEJ18	174	701802	1 - 671	15 - 685	BG119433, BG248347, BG109710, BE383397, BF310661, BF035847, BG111960, BE740887, AA872710, AW051637, BE904996, BE620053, BE294553, BG026514, BF036166, BE378983,

					<p> AV716604, AI300158, AV710056, BE257692, AW778814, BE879729, BE258999, AW592818, BE261359, AA044747, AA044799, AA878925, AI921790, AI469932, AA947927, BE251176, AA058505, BF245674, AA934688, BF310228, BE567185, AI299177, BF312584, BF243996, W38688, AI453622, AW749554, W95793, AI277337, BE271728, AA903577, AW874395, AI309289, AV712772, AI085685, AW118921, W95680, AI948425, AA934482, AI303007, AW601910, AI419931, BE440006, AW342036, AA053139, AW291750, N92290, AA962740, AW749576, AW954824, AV737047, AA055227, AV713230, AW749583, BF304421, T87073, AI371426, AV756120, AV681938, BE794262, AI143381, AI097662, BE258966, AA037518, N25835, AA912713, H71267, W80906, W80813, AA315305, AW374030, AW300889, AW300782, BF909052, AA037362, AI247237, BF336991, AA657605, AA541343, AA878777, W24468, T81887, AA054464, AW374000, BF216378, AI016169, AW374003, AA055226, AA213429, AW384982, BE067202, D20873, AI831636, AI038897, AW795930, BE327096, W31033, BF036705, W86895, BF792783, BF513528, T87074, AI361634, AI311824, BG036220, AW302965, AI307446, AI345737, AI345736, AV735576, AI345666, AI335476, BC000573.1, AK024569.1, AL136930.1, AL590002.7, AB060912.1, AL136754.1, BC008485.1, AL137294.1, AK024978.1, AL137459.1, AK000718.1, AF155827.1, AL117460.1, X72889.1, AL389939.1, AL080156.1, BC003104.1, AK000445.1, AK025632.1, AK000323.1, AB056421.1, AL080148.1, AL133104.1, BC007920.1, AL136747.1, BC006458.1, X86693.1, AL137523.1, AK026408.1, BC004951.1, AL050172.1, AL122098.1, BC008649.1, AK026642.1, AK025209.1, AB046642.1, AK025312.1, S77771.1, BC000725.1, AF002985.1, BC006119.1, BC008387.1, AL512746.1. </p>
HEEAG23	175	684254	1 - 1655	15 - 1669	<p> BF667852, AW798053, BG141339, AI279852, BG141348, H57654, AI472339, H85172, BF879975, BF879989, BF879974, AW954063, AW994019, BF590284, AA383569, H96534, BF800241, AA903404, AW873530, AA719530, AI084916, AW135894, AA993772, BF358415, AA890589, BG249829, W61170, AA807443, AW498471, AA814409, BG149771, AI828884, BE839816, BF954921, R76166, BE545018, AA470533, BF922076, AI829062, BE766575, BF808213, AA737653, H96878, R62923, AA714658, BF808212, AA705115, AI904064, AA569749, AI343340, AC004938.2, AL357033.19, AL121808.4, AL135749.3, AL359402.3, AC009314.4, AL031777.4, AL035079.14, AC078818.19, AL358612.8, AC018644.6, AL391839.9, AC013716.6, AC004882.2, AL078591.18, AL078645.31, AL031680.20, AL162505.20, AP001715.1, AC025264.16, AL109938.8, AC006312.8, AF243527.1, AL133367.4, AC010319.7, AC083875.1, AL050349.27, AL162615.13, AL356575.8, AP000223.1, AL121578.1, AC084732.1, AC005033.1, AC005082.3, AL136162.17, AC027319.5, AC062020.5, AL157915.3, U63313.1, AC006511.5, AC011443.6, AP001687.1, AC004477.1, AC011508.4, AC083866.2, AC006315.2, Z84572.1, AL136131.15, AC011005.7, AP001429.2, AL035462.21, Z83823.1, AC002350.1, AL138820.11, AC020896.5, AC010206.8, AC011495.6, D83253.1, AC004151.1, AC008813.6, AC005291.1, AL354696.11, AC005225.2, AC004652.1, AC083810.16, AL390071.9, AL021940.1, AP002907.2, AP000962.2, AL031721.1, AL031666.6, AL353807.18, AC004167.1, AL009183.10, AL356095.11, U78027.1, AC018763.5, AL021393.1, </p>

HEEAJ02	176	633657	1 - 1024	15 - 1038	<p>AL391114.12, AL121928.13, AC068799.14, AC004223.1, AC004846.2, AC002400.1, AC004867.5, AF141309.1, AC006101.3, AL390298.13, AL136297.3, AL035422.12, AL022100.13, AL355593.21, AC010374.5, AC011485.6, AL049643.12, AC008886.5, AC020916.7, AC005694.3, AL139385.12, AC003006.1, AL035659.22, AL022165.1, AC007066.4, AC022816.15, AC068312.4, AL133448.4, AL080243.21, AP000755.4, AC025430.5, AC011510.7, AC064878.9, AL139415.10, AL391137.11, AL356481.16, AC007561.4, AL133387.8, AC011900.6, AL137100.4, AC007014.1, AC067956.3, AL121712.27, AL121809.6, AL159191.4, AC069246.5, AC019171.4, AC004752.1, AL031427.15, Y18000.1, AC004832.3, AC066589.3, AC003065.1, AC073115.5, AC006028.3, AL353746.6, AC005800.1, AC090885.1, AC066515.7, AP001284.5, AC006011.2, AL035587.5, AC006017.2, AL121943.22, AP001698.1, AL445685.17, AC011477.5, AC018648.5, AL352979.4, AC016995.4, AC022401.3, AL133467.4, AL135978.4, AC004913.2, AC005387.1, AP000045.1, AL138707.10, AC023105.7, AC002039.1, AC018755.3, AC023137.5, AL117258.4, AC004076.1, AL513131.1, AC008844.5, AC018636.4, AL353657.26, AL031228.1, AL450344.4, AC006319.3, AD000092.1, AL157789.6, AC006049.1, AC011461.4, AL133284.13, AL121934.17, AL022316.2, AC008392.6, AL010677.4, AC006205.7, Z82244.1, AL139388.4, AL139322.13, AC012476.8, AC022415.5, AC068976.5, AC005393.1, AC006057.5, AC007324.55, AC020904.6, AC026464.6, AP001692.1, AP001724.1, AL139317.5, AC007003.4, AC009779.18, AP000963.2, AP000228.1, AC007919.18, AL499628.1, AC007051.3, AC010422.7, AC011718.2, AC006127.1, AL135927.14, AC007227.3, AC005696.1, AC004754.1, AL359236.4, AC026753.5, AC004534.1, AL356414.11, Z86090.10, AF107885.2, AP000547.1, AC010530.7, AC020740.5, AL162426.20, AC005488.2, AL034372.33, AP000689.1, AC037492.5, AC035409.15, AC005037.2, AL049793.4, Z97196.1, AP000140.1, AC009743.1, AP000359.1, AP000088.1, AL357312.8, AL590682.9, AA252707, AA252834, AL521986, AL521985, BG260084, AI817466, BE904098, BE894263, BF793132, BE873833, BF439331, BF983713, BF203429, BE910310, AI188184, BE904210, BG031216, AI803637, BE218333, BE378900, AW953618, BF667874, BF940993, AI479853, BG116696, BE747895, AI199381, AI423127, AI458395, BE389366, AA743927, AV728694, AV728921, AA780244, AA284556, AI138746, AW602172, AI340185, AI497680, AI701138, AA410675, AI949706, BF594730, AI570504, AI300375, AA262669, AA447624, AA423881, BF110364, AA400547, AA429108, AA316560, BF344873, AA042988, AA452960, AA284795, AI348309, AA043042, AA316842, AA451674, AA423902, AA400244, N80231, BF003113, AA042861, R76970, AA452820, AI571390, BE549542, AI560629, AA453218, H60916, AA868885, AA235589, AA496998, AW105644, AA448024, AA428872, BF589245, AA042849, AI654988, AA429062, AA357706, AW794510, R93695, T90652, AA523984, BF745192, R34969, BF087292, H83024, BE261946, AI869572, H51706, AA946612, W38322, R34866, AA044412, AA682182, T83180, R96730, R94542, T78530, AA962639, AA810439, BE382714, AA504714, AA367144, AA044398, H52424, H82805, W16760, AV660662, AI540890, AV727776, AV702804, AV706744, AV702994, AW961463, AW953965, AW950035, AV698087, AV721957, AV706987, AV652443, AV703263, AV706775, AV706915, AF113126.1, BC000557.1,</p>
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HEEAQ11	177	777843	1 - 907	15 - 921	<p>AB029821.1, AF176807.1, AF176806.1, AC020358.4, AF294468.1, AF294465.1, AF294460.1, AF294464.1, AF294466.1, AF294463.1, AF294467.1.</p> <p>AW572915, BE500968, A1631708, BF056783, A1638675, AW024125, AA812885, AA911102, A1651682, AA758532, AA934362, AW104268, AA68716, BF223496, AA496078, AA608859, AA973942, AW418725, BE041425, AA931770, AA513329, BF056762, AW975618, AW949645, AW964468, AW966389, AV724520, AW966330, AW973541, C14331, AW960553, AV718692, AV702035, D80195, C14389, AV718489, AV719468, AV718800, AV719822, AV719324, AV718707, C14429, AV718931, AW366296, AA305409, AW966534, D59619, D80210, D80166, D80240, AW973488, D81030, AW949656, AW949642, AW965185, AW965197, AV702211, AW966075, AW978634, AV723927, AW966065, AW949653, AW962245, D80212, AW966053, AW959799, AW978634, AV723927, AW966065, AW949653, AW962245, D80212, AW966053, AW959799, D80219, D59859, D51423, AW973474, AV699550, AW966050, AV719783, AW975613, AW965196, AW965184, AW978661, D51799, AV720464, D80253, AV718770, AV720731, AW966029, AW973307, D51060, AV718938, AV718633, AW975605, D59610, AV720878, AV719557, AW960465, AV699447, AW958993, AV722801, AW973334, AW959136, AW966531, AW949646, AW949654, AW959202, AW966013, AW960473, D58283, AW966022, D80022, D80366, AW964756, AW975621, AW964477, D80188, AW966041, AW965163, D80391, D80164, AV718844, AW959582, AW966054, AW966059, AW958992, D59787, AW978648, D59502, D59467, AW949631, AW949643, AW949618, AW949655, D59275, AW960454, AW973330, AV720791, AV720203, AV719188, D80043, D80227, AW966062, AW956434, AV718440, AV720028, AW959597, AW959628, AW965177, AW959570, AW973485, AW965175, AW973482, AV700229, D57483, D59889, AW959062, AW964488, AW949641, AW962082, AV699927, AV738340, AV723097, AW966043, D80269, D80196, C15076, D80024, AV699866, AW949658, AW949657, D80241, AW956397, AV699746, AW949629, D59927, AW375405, AW964737, AW973447, D80038, D80193, D50979, D50995, AV700889, AV744690, AW949630, AW966030, AV720150, AV721386, AW965158, AW949633, AW949632, AW966032, D80378, D80045, AW753053, AW966023, AV718530, AV720812, D51022, C14014, AW960532, AV701004, AW960504, AW959469, AW960504, AW177440, AV744012, AV720533, D80248, AW975623, AW973490, A1905856, AV701125, AW752082, AW962395, AV701166, AV701149, AV703738, AW973445, AW964532, AW966368, AV720151, AW966397, AV720220, AV705869, AV720616, AV742732, T03269, AW973465, C75259, AW960570, D80133, AW178893, AA305578, AW966369, AV699669, D80302, D80251, AW973473, AW965176, AV727978, D81026, AA514186, AW966378, AW966386, AW966331, AW966398, AV706147, AV719913, AV720654, AW966399, D80522, AL121894.26, AF058696.1, AF271371.1, AB028859.1, X67155.2, D34614.1, D88547.1, AB002449.1, D50010.1, AB038216.1, U79457.1.</p> <p>AV653338, A1150047, AA335017, AA335685.</p>
HEEB105	178	130761 1	1 - 880	15 - 894	
HEGAH43	179	532596	1 - 428	15 - 442	<p>AA400429, AA994981, AA846419, AA453384, A1015471, AA992965, AA400538, AL360078.16, AJ236910.1, AJ236909.1, AF327147.1.</p>

HEGAN94	180	885637	1 - 568	15 - 582	AI018488, BF509739, AL157823, 9.
HEGBS69	181	109334 2	1 - 795	15 - 809	BE041526, BF514935, BF515526, BF515928, AL656756, AL138127, AI150056, BF510812, AW165981, AI360220, BE963568, AL512683, 1.
HELK31	182	681138	1 - 1382	15 - 1396	AL519840, AL519839, BE379142, BE786389, BE796190, BG117991, AL524590, BE744597, BE909841, BE907873, AL043167, BE544763, BE740216, AL518390, AL529705, AW592682, AW874363, AI085412, AW958434, AU126873, BF132076, AA604374, BF541758, BF794982, BE545432, AA936378, AA161264, AA531252, BE563799, AW072533, AA639981, AA677594, AI138280, AA218539, N94446, AI363012, BF114843, AI083837, DS1047, BF343738, AW499697, AA437204, AA132746, AV712240, AI086913, AA889889, AA161263, AA916429, AA142878, AL518389, AA810233, AA613892, AA424834, AA143152, AA603133, AA132651, H11615, AW367012, AI268931, AI955333, AA948407, AW327686, AA856621, AA227183, AA524602, BE537412, W30793, AA969047, BE875215, AU149648, R54573, H18393, AW080718, AI082408, AA354603, BG024936, AA807409, BE762990, AA225683, AA745633, R09626, W22670, AA296971, N79058, AW131898, AA283047, R09625, AA974359, AA216343, AW352289, AI014772, AA426455, AA335199, AW352287, AA876045, AA569616, AA426587, AA365881, BE645623, AW352294, AA218538, AA225708, AW149303, Z45742, AA298844, AA693654, Z41394, AI740665, BE142815, R09514, AW263934, BF515182, AA652379, W24000, AI400292, BF893436, AA281197, AI376646, AV703989, AV725633, AV656373, AV702372, AV702417, AV704217, AV702280, AW954248, AV702998, AW950443, AV725991, AW960601, AW952403, AW952410, AW952183, AW954237, AW952751, AW956075, AV645936, AV709587, AW955723, AV658084, AV692600, AV650315, AV659389, AV697880, AV727613, AV726010, AV660258, AW959521, AV647789, AV708109, AW956474, AV659294, AV727787, AV703146, AV725745, AV686060, AV660608, AW951239, AV728148, AV726590, AV656478, AV709314, AV653353, AV654070, AV691080, AW951281, AV702385, AV702772, AW949802, AV658275, AV652001, AW955662, AV703669, AV707979, AV725208, AV727003, AV709580, AV725582, AV708786, AW957517, AV659547, AV727526, AV651920, AV725618, AW954439, AV706734, AV729076, AV702266, AV725577, AV725033, AV706223, AV728924, AV725617, AW954206, AV707863, AV696931, AV707798, AV703062, AV727822, AV707572, AV699089, AV705135, AV701874, AV703501, AW962444, AV707401, AV701183, AV709660, AV704585, AV654035, AV709935, AV707652, AV728721, AV707654, AV707663, AV683994, AV704042, AV654282, AV697288, AV729220, AV709880, AV687035, AV698290, AV704847, AV694836, AV706882, AV697498, AV702954, AV727238, AV686420, AV694812, AV682997, AV696866, AV727126, AV707656, AV655890, AV728997, AV706162, AV705635, AV686390, AV702794, AV656256, AV686417, AV686083, AV698429, AV656240, AV655577, AV694871, BC001239.1, AF201931.1, AK001341.1, AL136674.1, AL137878.1.1, AF217994.1, Y08991.1, Z30183.1, U94592.1, U45328, 1.
HELHD85	183	847372	1 - 1872	15 - 1886	AI284640, AL138265, AL046409, BF677892, AW193265, AV760937, AW969629, AI431303, AV760777, AI613280, BG249643, AW407578, AI281881, AV763354, BF130107, AI345654,

	AW728425, AW502975, AW965008, AI334443, AV710066, AW419262, AI350211, AI801482, AW473163, AW238278, AI754658, BF668217, AF3530238, AI754253, AV762139, AI963720, AV725423, AV728928, BE895987, AW303196, AW274349, AL119691, BF681427, AV762098, AI133164, AW438643, BF827410, AA581903, AW970848, AV762009, AI270117, AI076616, AW301350, AL045053, AW265393, AW021583, AW833862, AV7276435, AI138455, AW974109, AW439558, AW327868, AV762050, AV729960, AL041690, AW276827, AI890348, AI567076, AV761362, AL044940, BG109996, AW004911, AF074677, AA720702, AV764578, AV761489, AI305766, AW500125, BE047069, BF970654, AU145393, AV735495, AW731867, BG236735, AV764398, AI421841, AL042753, AW960468, BE206443, AI624142, AA621858, AV761925, AV759172, AV702857, F36273, BG222267, AI164251, AI799042, AI249997, BF793664, AU147104, AI708009, AV763971, BE389111, AV734666, AV762067, AA491814, AV761106, BF697673, AI434695, AV740801, AV759117, BF241967, AW265385, AW062724, AV763122, AW265009, AI037683, AW103758, BF940837, BE350475, AI305547, BF475381, AL121235, BF337291, AI192631, AI821271, AA469451, BF942454, AL042420, AI341664, AV710774, AI053672, AW973397, AI623720, AI903462, BF680074, BF793766, BE674881, AV763550, AL048925, AV760042, AW073470, AI679782, AL046205, AW963497, BF681576, AI457397, AW662543, BF797630, BF592311, AI471481, AA610491, AW088846, AV733830, BF9655007, AA526787, AV759505, AV730310, AW302013, BG036665, BF541116, AW301809, AV764530, AL038474, AV761631, AW021207, AV762959, AV762395, AI289067, BG171096, AW270382, AV763633, BE042649, AW338086, AA491284, AA908687, AA551552, BF674620, BE160516, AW410400, BG178002, AI133102, AW083364, AW872676, AW088202, AI919265, AI801600, BF792870, AW979060, AV762535, AA630362, AI119984, AI688846, AA631507, AI537506, AV743472, AI801591, H56509, AA584145, AI123309, AV732865, AV764329, AA521323, AI937850, AW574794, AU145711, AP001423.1, AP001731.1, AP000021.2, AP000163.1, AC004765.2, AL1391803.14, AI122001.32, AI139809.16, AL354932.26, AC006128.1, AC018720.5, AL160155.19, AC005696.1, AF207550.1, AE006462.1, AL158207.15, AL022315.1, AL513008.14, AL121904.13, AL022313.1, AL356299.16, AL450226.1, AF077058.1, AL023575.1, AC006483.3, AL049758.11, AF129756.1, AC009412.6, AL136418.4, AL139054.1, AF196969.1, AC010422.7, AC011497.6, AC073593.13, AI139230.25, AC005295.1, AL136980.5, AL162426.20, AC005808.1, AC007536.9, AL121903.13, AC000397.1, AL355871.5, AC073073.2, D83989.1, AL353135.32, AC009470.4, X75335.1, AP002906.2, AC018637.3, AL359457.12, AC011495.6, AL139396.17, AL354707.17, AJ4000879.1, U78027.1, AL049830.3, AC018751.30, AC009516.19, AC000041.2, AP000114.1, AP000046.1, AL355543.13, AC005324.1, AC008770.6, AC008736.6, U91323.1, AL118520.26, U66059.1, AL390205.17, AC005291.1, AL035422.12, AC008543.7, AP001781.4, AL121653.2, AC009228.4, AL035071.17, AC027644.9, AC010404.5, AI133153.3, AC005740.1, AC009269.6, AL161656.20, AC002996.1, D84394.1, AC079177.21, AC011489.6, AC006285.11, AC007919.18, AC007620.30, AC073138.3, AC009756.9, AP001717.1, AL031848.11, AF015151.1, AC090939.1, AC005839.1,
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HELHL48	184	696945	1 - 2957	15 - 2971	AL529435, AL524123, AL524122, BF312538, AU129727, BG164871, BF348048, AU120482, BG167168, BE733600, BE876571, BE875645, BE296592, BE901138, BF343028, BF308771, BF345199, BF308189, BE336871, BG028125, BF115264, BG116986, BG249650, BE903726, AV728373, AW007132, BG121227, BF206051, AW963600, BF347698, AU151806, BE294229, AW303548, AW411067, AW967356, AW411066, AU128086, AA100522, AI867409, AU137055, AI378902, W28880, AW752755, BF308950, AW751506, AI421175, BG180673, AW590377, BF001722, AI872412, BF924126, AA180518, AI373035, AW179322, AI401197, R24305, AW178945, AW150193, AA209515, AA564224, AI370802, AI984047, BF438508, AA293441, AA088551, AJ758667, AI275100, AW996404, AW007984, AI800710, AU150189, AI361596, AU150403, AA669849, BF432420, AI559326, AU146534, AA514455, AW513096, N31325, BF754347, AW896670, BE789836, AI299591, AI272929, AI089779, BE008621, AI912569, AI276235, AI283742, BF939706, AA508685, AA180517, AW169281, AI688823, AI310354, AW007978, AI359948, AA148446, AA292742, AA478976, AI041725, BE790438, AA292741, AI221864, AI157827, AA552023, AA112746, AA513477, AA232508, AA148445, AI493536, BE206110, N26490, BE147464, AA293508, T84545, BE093924, BF884193, AU157002, F12444, AI348568, D31225, N47540,

					<p>AI269318, BE147790, AA088385, T74066, AA053180, H30187, AA654655, BF154572, AW579667, T88004, T35342, AI074255, AW571550, BG055222, AW579684, Z39831, BF434566, AW390755, AV698355, Z43770, AV685886, BE463536, AW270979, AW378596, AW514887, T31997, AA863225, BE296813, H04167, AI246176, AA365514, AA513359, AA477913, T34879, BF347090, BF438580, AA151938, AV684774, AA336395, AA492462, AW009840, AA053627, BF906710, T87910, AI470954, BF814719, BF593969, T64888, AA136495, AA179793, H08606, AA907036, F10066, AA503814, R22025, AW577064, BF749344, AA298224, AA339096, AA079476, T35287, AA936508, AI620090, AA079475, AW378971, T39180, F08643, H08605, AA372556, AA995437, BE294737, AW300420, AA496416, R01535, BE311798, AA345134, R44902, R22078, F02150, R49987, BE840622, T35182, AA369833, AI244019, BF947140, R00876, BE840609, BE294732, H04166, AA887342, BE143234, N47539, AW374684, T31964, AW178632, AA635427, AA188708, AW582129, R47850, AA152055, BF476766, AW291610, AA369871, AW451289, BE467357, AI630981, AW134630, BE763447, AI383035, BG255592, T58576, AA248989, BC003128.1, BC006200.1, AK001112.1, AL161962.1, BC000035.1, AK001524.1, AF151847.1, AK001424.1, AL359542.13, AL034405.16, T58537, AA232607.</p>
HEMAM41	185	741647	1 - 1323	15 - 1337	<p>AL515525, BF966744, BF793066, BE905040, AV697070, AW157314, AI816071, AL515524, AW261874, BF966307, AW163370, BF727408, AW151173, AW001897, AW236835, AW235694, AI801254, N62855, AI815990, AW117364, AW976507, AW150293, AA876913, AI635914, AW79526, AI584106, R40658, D12158, AW148443, AA338451, AW166670, AI245076, D12218, AA7369838, D57788, AW631476, AA969485, AC021086.4, AC027315.3, AC010382. 4.</p>
HEPAA46	186	596830	1 - 1115	15 - 1129	AA835052, AI220434, AA335178, AA905529, AL031650. 22.
HEPAB80	187	130779 0	1 - 785	15 - 799	AW274007, AI677890, AW510786, AW468943, AA335322, AI807924, AW172560, AC006116.1, AC011506. 3.
HEQAK71	188	598018	1 - 1675	15 - 1689	<p>AW960453, AA577682, AI740956, BF589404, AI810888, BE894896, AI129260, AI743307, AI953066, AI017271, AA631231, BE503649, AI400945, AI670754, AA534344, BE765639, W72296, BE673403, AI188476, AW264555, AW880277, AW305140, N54915, AA917732, AI439508, BF510644, BF984766, AA088886, AV750742, BG109860, BE765623, H01968, AA573814, T69918, AI758231, AI479210, AW138022, AV751020, BF437113, N40587, N25881, R36078, BF989181, BE897314, BF574472, AL036615, AL117461.1, AK026979.1, AC011093.6, AL359709.15, AP001437.1, AP000011.2, AL390798.3, AP001728.1, AC005345.1, AP000153.1, AL078645.31, AL137021.15, AC004817.2, AL357117.20, AL442183.4, AC004830.1, AL354696.11, AC003013.1, AL138743.5, AL513023.12, AC012405.5, AK027165. 1.</p>
HERAR44	189	566811	1 - 406	15 - 420	AC007358.2.
HESAJ10	190	526013	1 - 1076	15 - 1090	<p>BG163863, BF973568, BE905545, BE440123, BE877406, BE878414, AI810399, AA421950, AW954926, AI826072, AA507017, AI597673, AA147367, W46280, AA586621, W70172, BE879100, AA595444, AA725205, AI701337, AA421951, AA722808, AA988274, AA844455, W96316, T59591, BF869408, BF858292, BF858296, AA587061, AI077904, BF858302, AA147419, AA058506.</p>

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HETBR16	192	703243	1 - 1555	15 - 1569		AW661837, AI127395, D62246, BF838051, AA363498, BF673053, BF838050, N68223, AA608520, BF78696, AW238127, AA570224, AI635819, W45298, AW949001, BF932686, BE063025, W45283, BE063030, BF815072, F31654, AI610607, AI640411, AA568947, BE049229, BF856556, AI679442, AI679952, BF857619, AA665645, AV656064, AW949012, AA653612, F27410, AV740009, AI889440, AI540408, AV720211, BF850690, AA605266, BF844769, AW261996, AI885488, AA494090, AA626402, AW020088, AA486970, AW167154, AI809818, AA745356, AI634601, BE162124, AW271917, BE179216, AI859280, AU158549, AW148386, AW971243, BE674880, AA661948, AA665330, AA649148, D82461, F31619, AI565245, AI932902, AA708213, AC072052.6, AL021807.2, AL132718.5, AL132653.22, AP001417.2, AP000160.1, AI122023.3, AL391987.15, AL162385.16, AL390295.10, AP000018.2, AC008122.15, AP001730.1, AL078475.2, AC090051.8, AL132838.4, AL050302.2, AC006026.2, AC004964.2, AC008745.6, AC019274.5, AL163203.2, AC002115.1, AL139809.16, AL139317.5, AL118524.25, AC004098.1, AC006387.3, AL033529.25, AL360219.18, AL163210.2, AC011455.6, Z98048.1, AC007637.9, AL021408.1, AL353679.18, AC021019.5, AC005668.1, AC011497.6, AC010150.3, AL135839.15, AL445490.6, AL033378.12, AF258547.1, AE000658.1, AL133545.10, AL031666.6, AL157829.24, AC020601.10, AC007055.3, AC003029.2, AC007881.4, AC007954.7, AC022407.6, AP001746.1, AB020878.1, AC007055.3, AC003029.2, AL158089.8, AL391384.18, AL352979.4, AC073964.3, AC023668.4, AL356805.5, X87344.1, AL445466.9, AL590043.7, AC083875.1, AC012592.10, AL161938.6, AF258545.2, AF084941.1, AL008723.8, AC011604.10, AC090842.1, AL359238.4, AC018448.16, AC004066.1, AL354707.17, AC068948.1, AL354797.16, AL035671.5, AL050335.32, AC003954.1, AC010620.4, AC021016.4, AC005666.1, AL135927.14, AC007227.3, AC008625.5, AC008521.5, AL022717.1, AC019171.4, AL356782.14, AC003106.1, AL034349.3, AL035587.5, AC007263.4, AC010422.7, AL583856.6, AC004671.1, AC010976.5, AC011471.6, AL162274.17, AC005899.1, AC005406.2, AC023355.5, AC004686.1, AF008243.1, Z94801.1, AL390252.9, AL031734.9, AF015416.1, AL158040.13, AL354993.24, AC005670.1, AL121891.22, AC073838.6, AC005000.2, AC005971.5, AL137230.3, AC009086.5, AL137853.12, AC018828.3, AC006211.1, AC002985.1, AC005209.1, AC022383.3, AL445196.7, AL109946.12, AC011494.2, AC022384.4, AC006500.4, AC008645.4, AC015968.4, AC006353.3, Z85999.1, AC006017.2, AC018832.4, AL160269.14, AC068492.2, AL355595.10, AC005399.19, AC010267.6, U80017.1, AC016598.5, AC005411.1, AC000385.1, AC003041.1, AC011479.6, Z97630.11, AC004881.1, AC008770.6, AC016770.10, AF111168.2, AL133406.14, BE645551, BE304956, BE048918, BE740087, AW960605, BE207572, AW195635, AA177001, AI824341, AW362246, BF591120, AA578987, AA425334, BF002699, AI681859, W37110, AA991211,
HETLM70	193	117751 2	1 - 1237	15 - 1251		

HFABG18	194	847073	1 - 1331	15 - 1345	BE859016, AW150693, AW611712, BE179770, BE927270, AI357925, BF038466, AW173702, BF748385, AV724505, AW102565, AW751971, AW748813, BF515478, AA559207, AW601591, AW001725, HI13734, AI908541, BF516168, AA426447, BF090860, AA919025, BE830375, AI686245, AA335628, AA160404, AI521130, AA147206, AI689513, AI699743, BE709540, AW751973, AA906975, AA926906, BF855782, BF872555, AW664454, BF765954, BF090962, BF570393, BF569907, BF344166, AA758023, W63573, AA877107, AW664584, AI924890, BE207784, AI422142, AI811174, AI891097, AI379416, AA631138, AI129321, AA233722, AA861574, AI339443, AW009533, AA635649, AA910314, BF510307, AA948287, AA421401, AA621181, H52254, AA908447, BF127938, AA330666, AA458586, AA328941, AI472877, BF337899, AA853185, R69866, AA852144, BF999691, T49327, AA677036, AW024548, R46515, R69911, BF999694, AW593365, H52351, AA976306, BF903330, T49326, AA233143, AI381786, BE827715, AA359077, AI569251, AI685425, AI826541.
HFAMB72	195	490697	1 - 1309	15 - 1323	AW897798, AL044056, W44681, AV758808, AW057713, AI445728, AI694501, AI567918, BF929670, AW137633, AI362734, AI560113, R66361, AA973346, R24468, AA256199, R24469, M78793, AA987235, R67503, BF926218, AA688372, AA398164, AA861041, AI024099, AA719008, AI694956, AI150346, AI217933, AA459841, BE217862, AA393248, AI652522, AA629029, AW137492, AI075905, AI796754, AF081250.1, AF081249. 1.
HFAMH77	196	543486	1 - 655	15 - 669	AI340312, BE676214, AA778534, AW300884, AI609950, AI340016, AI632085, AI335706, AA768117, AW027671, AW978490, AW590880, AW589742, AI272784, AW027648, AA983621, AI421130, AA918495, AI280887, AA724472, AA830837, AI024114, R60771, AI675916, N94357, BF960835, BF953963, AW572683, AI159997, AW772189, T05324, W52231, AI394585, F35349, AI445605, AI347406, R49581, AW020397, AB051512. 1.
HFCCQ50	197	579993	1 - 1257	15 - 1271	AL522683, AL522684, AI628729, AA133340, AW139771, AI690104, BF195450, AA133381, AW207332, AI267992, AI961337, R41690, AB049586. 1.
HFCEW05	198	561560	1 - 919	15 - 933	AI674710, AW075264, AI572441, AW665201, AA975502, AL134012, AL359582. 1.
HFFAD59	199	520369	1 - 456	15 - 470	AV699250, AV662248, AV699269, AV719565.
HFFAL36	200	560639	1 - 1006	15 - 1020	AL537384, AI656961, AI651790, BE466895, AA481913, H54148, AW020416, AA524615, AI309941, T82299, AW971340, AI625683, AA007579, AA670123, AW088680, AA112001, AI250970, AI613405, AI376500, BF526521, AA480105, AA417299, BF054867, AI016470, AI373731, AA416675, BE622947, AI340568, BG180542, BE222669, AI266504, AI291507, AI672420, AI650382, BF885229, AA129526, AA081857, AV699196, AV699199, AA948596, AV699131, AV699223, AV662288, AV699219, AV699246, AV662257, AV699269, AV699218, AV662235, AV662248, AV699182, AV699250, AV662242, AV699204, AV699137, AV699147, AV699098, AW963961, AV699123, AV662247, AV662223, AV699144, AV699170, AV699136, AV699224, AV662272, AV699125, AV699203, AV699200, AV699247, AV662191, AV699255, AV662185, AV662196, AV662317, AV662287, AV699236, AV726209, AV652214, AV650926, AV652066, AW956240, L48842, AF051321.1, AF051322.1, AF069681. 1.

HFGAD82	201	513669	1 - 1867	15 - 1881	<p>AL119979, BF346635, AV726399, BF035097, AV727342, AL119977, BF920864, AW888751, N31682, AW148844, AA72781, AA326677, N23200, AW961610, BF976989, BE765872, BE765750, BE765749, BE765443, BF570590, BE765618, BF438771, BE766953, BE766490, F06586, BG057153, R60278, F07047, AA628815, AV722183, R16237, BF364146, AA204942, AV734361, N71200, AI000462, R54067, Z40722, BF337123, R54066, AW903171, H24278, AV726415, H16893, AW897545, H16783, H22887, R16238, F03521, R42035, F05678, T80483, AA321847, AV731162, AV731097, AV730504, AV730299, AV731130, BE763530, R20855, AA386266, AW890775, R45969, R42611, N94832, R39831, F02857, F03323, T03048, R11992, F07675, AU118413, AW890773, AA640468, N95708, F03679, BE830656, BF948144, M85660, AL119687, T08757, AV722325, AW904904, BF344999, AI003266, N76471, N47227, AW903272, BF977690, T53097, BF918689, F01937, N58994, AI000789, AW898733, BE702498, BE699153, AL118827, BE708346, F07242, AW897547, F01938, N51309, AC003037.1, AC022486.4, AC007379.2, AC007064.27, AC006548.20, AC016752.2, AC008175.2, AC007965.3, AC007322.4, T66696, T66697.</p>
HFIIZ70	202	104335 0	1 - 1394	15 - 1408	<p>AL048246, BE877406, BE905545, BE440123, BF973568, BG163863, BE878414, AI810399, AA421950, AW954926, AI826072, AA507017, AI597673, AA147367, BE879100, AA586621, AA725205, AI701337, AA595444, AA421951, AA722808, W46280, W70172, AA988274, AA844455, BF869408, W96316, BF834026, BF858296, T59591, BF858292, AI077904, AA587061, AA058506, BF858302, AA147419, AA649904, AA651755, AW579978, AW383857, AI734990, AI077596, BF858301, AA034247, R24354, AA576389, AA054465, AA814555, BG170925, W69907, AI918084, BE833571, BE159104, W96221, AA326962, BF339936, AA319027, AL048247, AA626906, AA897619, AI826118, AA683597, BF363870, AA932608, AA046341, W32814, BF858297, R24251, AA046263, AA630968, AW750463, AI146631, AI270350, AI074824, AI074849, AI081420, AI086654, AI934162, AW029263, AI675825, BE964767, AI886181, AI799183, AI620302, AW268243, AI634450, AI334450, BE968711, AI540458, BG251257, AI699011, AW268220, F27788, BE733009, AI336575, AW129271, BE964497, BG025209, AI345148, BF817418, BF344652, AI627896, AA983883, BF816455, H42825, BE967255, BF343172, AI812080, BF055742, AI613548, BF814360, AI336494, BE963918, AI452993, AI520931, AI345229, AW302854, AI349798, BF924856, AW168485, AI699862, AI073952, AI349004, AW152469, AW149925, AA494167, BE897632, AI335209, AW961463, AI859464, BG254754, AW271119, F37450, AI687166, AI784230, AW403717, BF987104, AW172723, AI891157, AI480118, AI805638, AI933589, AI811644, AW303089, AI680457, AI783861, AI434741, AW083804, AI251830, AI828731, AI924971, AW268306, AI612759, AI648663, AW022682, AI566630, BE393551, AI537617, BF812963, BF817402, AI119319, BF921092, AI499285, BE613727, BE965724, AI446248, AV716516, AL038605, AI680162, AI475408, AI682841, AI568114, AW193872, AI537024, AI866465, AW193843, BF970449, BF032768, BF812938, AI567351, BF764538, BE966990, AI538342, AI620003, BE544111, BF895953, AI610645, BG112239, AI432040, AI866127, AI568138, AI445992, AI922550, AW162189, BG027628, AA493923, AI927755, AW079159, AW117746, AI244380, AI539711, AI866573, BF909758, AV682124, AI567582,</p>

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HFKE18	203	889515	1 - 2393	15 - 2407	BC003650.1, AL133093.1, AF217966.1, AF061943.1, AB060883.1, BC009310.1, AB055374.1, BC004256.1, U58996.2, Y10080.1, AB050533.1, BC008417.1, BC007641.1, AK026746.1, AB063084.1, AB063077.1, AF061795.1, AF151685.1, AF217991.1, BC008078.1, AK000486.1, AL050092.1, BG110420, BG115334, AI185642, AW611548, AI65744, AI049960, BF206049, AI884824, AI760384, AA603803, AI990152, AI991071, BF512789, BF1111782, AI653741, AA425329, AW411097, AI934872, W87427, W38311, N46445, N81109, AI061327, AI500218, AI365116, AW235906, AA426444, AW590032, AA922999, AI675005, BE538807, DI9613, W67792, AA515114, W67850, N79808, AA903500, BF310800, AI363322, AW675761, AA806029, AA856723, AI049728, AI653583, AA911610, R21297, AI040049, AI889471, AI368191, F08500, BE730105, AW196227, AI890737, BG258747, BE220526, Z39142, N70816, AA749162, AA258815, AA665599, T79989, AI193425, AI970238, BE781345, AI216679, F04714, W01450, AA349299, BE252937, AI696235, AI915010, R46143, AW937426, AA761144, N48946, ZA3036, AA912452, BE177220, AW613925, BE543843, BF307683, AI472495, AI954525, BF821897, BF821009, AA937427, N64587, AF055012.1, AL050318.13, AB042646.1, DI6966.1, AC005157.1, AL080249.26, AL136313.27, AC002492.1, AL139415.10, AC020947.6, AC005412.6, AL109823.23, AL035413.19, AL021391.2, AC011742.3, AP002851.2, AC016601.6, AC007731.14, AL158040.13, AC010654.8, AC007272.3, AP001712.1, AL389888.8, AC007226.3, AC010326.6, U17296.1, AP001717.1, AL033529.25, Z93930.10, AL118520.26, AC005500.2, AC011467.7, AL132777.4, AC005180.2, AL121601.13, Z99716.4, AC018644.6, AL022165.1, AP001745.1, AC002115.1, AL133545.10, AC009412.6, AL121751.12, AL136123.19, AC006965.3, AL121747.41, AC005052.2, AC005899.1, AF219991.1, AC010463.6, AC004089.25, AL356299.16, AL365505.15, AC006312.8, AC024563.4, AP001670.1, AC005971.5, AC013717.8, AC005081.3, AL121972.17, AC007934.7, AC007055.3, AC011737.10, AC006241.1, AL035415.22, AC005722.1, AL049780.4, AC044797.5, AL137792.11, AL359091.10, AL138836.15, AC004000.1, AC007237.3, AC008925.3, AL033392.5, AP001621.1, AC006211.1, AC018758.2, AP001693.1, AC005015.2, AL133485.3, AC007199.1, AC006084.1, AC011544.6, AP001716.1, AC008569.6, AL034420.16, AL049776.3, AC009004.6, AL049867.2, AP003357.2, AC012476.8, AF134726.1, AP001727.1, AC005098.2, AC008755.6, AL121653.2, AC006511.5, AC011475.6, BE222940, AI479528, AW242860, R46796, M62053, AI017670, BE048467, AI671740, AW001738, AA351031, AI206414, AF124373.1, AB009698.1, AF104038.1, AB009697.1, AF057039.2, AP001858.4, AJ249369.1, AF097490.1, AJ251529.1, AJ271205.1, BF592863, AW594700, AC090945.1, AC009508.3, AL390068.12, AP001422.1, AP000021.2, AP000162.1, AP001731.1, AC079950.23, AC005670.1, AL138690.19, AC010163.7, AL520282, AI804338, BF951545, AW206420, AI039803, AI362891, BE699734, AA410892, M79026, AA419536, H47046, AA082306, AL520649, BF951672, BF944123, AW904559, BE702538, BF944119, AW954591, BE935929, Z45619, T79873, AB023185.1, AU119532, AW976010, AV762220, BF792326, AV760760, BG164166, AL037632, AU117926,
HFKEFG02	204	634743	1 - 781	15 - 795	
HFOXB13	205	570699	1 - 1155	15 - 1169	
HFPAC12	206	589522	1 - 1074	15 - 1088	
HFFPA071	207	629193	1 - 2053	15 - 2067	

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HFPCX09	208	130979 3	1 - 2199	15 - 2213	AL536594, AV721181, AL138260, AW182261, AW590515, AF621238, AA992136, A1039940, A1240096, BF475263, A1989349, AA992473, T15408, A1918747, H05529, H46336, R44821, R45685, H12939, AA296979, H05383, H05384, C14158, A1802297, D45285, R14994, H10614, H46267, AF055636.1, AL157396.9.
HFPCX36	209	526635	1 - 782	15 - 796	A1085242, A1440117, BG012020, AA659232, AA131088, AC006160.9, AC006449.19, AC020904.6, AC018711.4, L44140.1, AP001760.1, AC004983.2, AC005529.7, AL135744.4, AC005527.3, AC083868.2, AC051619.7, U91323.1, AC008623.4, AC023510.16, AP001718.1, AC020916.7, AC018801.4, AL049776.3, AC006006.2, AL355343.18, AC067941.7, AC011731.8, AL356805.5, AP000501.1, AL139021.6, AC018828.3, AC006205.7, AE006467.1, AC007263.4, AL121658.2, AC005409.1, AC022415.5, AL121983.13, AC005089.2, AC020983.7, AC004491.1, AP001830.4, AL162615.13, AC009412.6, AL049709.18, AC018808.4, AL138741.13, AC022443.4.
HFRAN90	210	520368	1 - 518	15 - 532	AV705871, AV702196, AW965899, AW950678, AW959842, AV727499, AV705836, AV709248, AV728351, AV705453, AV728953, AV727766, AW963219, AV705697, AW956780, AW958316, AV726243, AW958045, AW956792, AV703742, AV726617, AV727120, AW956797, AV727144, AV705340, AV721818, AW964578, AV708025, AV705221, AV685113, AV707804, AW963399, AL536138, AL535660, AW966491, AL557799, AV725783, AV655703, AA585430, AV701667, AV746191, AW957853, AV728973, AW963378, AW959956, AV661824, AV741949, AV753624, AV726270, AW950597, AV701071, AW962407, AV727361, AV738232, AW951204, AV726551, AV731131, AV726328, AW961409, AV724091, AV707353, AW953763, AV729557, Z28355, AL547039, AW950644, AW954994, AW963350, AW965898, AA170832, AV702345, AV727828, AW955629, AV729198, AW964540, AV707331, D61254, AW963631, AV688541, AV702601, AV703620, AV712504, AW952064, AV717687, AV715667, AW955719, AV728210, AW954141, AW961831, AV692516, AV702095, AV705319, AW957300, AW959059, AW958033, AV762741, D60765, AV651281, AV745417, R45895, AV727449, AV732203, AV732299, AV732336, AW950971, AW950004, AV730119, AV730216, AW949940, AV707733, AV730546, AV730062, AV730115, AV731078, AV732566, AV702146, AV730609, AV701283, R28735, R29445, AV752043, AV731977, AV725497, AV730781, AV731694, AV731043, AV730288, AV732002, AV723449, AV723273, AV732149, AV732155, AV732255, AV752443, AV701626, AL557264, AW961578, AV729378, AW962864, AW957318, AW950689, AW955905, AV684604, AW965730, AV709733, AV728818, AV699199, AW965749, AW967047, AV699182, AV699139, AW950531, AW952395, AV701183, AV728312, AV704490, AV728884, T18597, AV709555, AV727954, AV729076, AV701088, AV703972, AV731411, AV649758, AV658784, AV705185, AV702191, AV729348, AV728642, AV705548, AW949437, AV658448, AW961112, AV723874, AV730165, AV725432, AV701311.

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HFTCU19	211	735139	1 - 1561	15 - 1575	AL522686, AL532414, AL528017, AL525764, AL525713, AL517601, AL532413, AL517602, BE728855, BE728429, BE790819, AL522685, BF793544, BG035367, BG250928, BG248668, BE620516, BG261214, BF527519, BE744785, BG027945, BE875302, BG107554, BE272944, BE274274, BE728950, BG104319, BE272684, BF025761, BF568694, BE408005, BE892043, BE259455, BE728885, BE786141, BE272952, BE298531, BE263890, BF965267, BE786762, AW249086, AA773582, AW956716, BE896833, AW248651, BG028978, BE272544, AI301926, BE514887, AW958043, AA707330, BF116072, BE301937, AW328603, AW958038, BE546423, AI983484, AI336123, BE409785, AI094652, AA857454, AA534610, AI301124, BE218758, BE391518, AW026133, BE220235, AA039645, AI826760, BF132535, BG164328, W07685, AA143751, BE217896, BE042731, AW800820, BE265135, AA316625, BF897135, R80333, AA143714, BE965179, AI371146, AI299006, BE859048, AA181066, AI273416, BE265826, AW328604, AI033743, AA209410, AI862384, AI989356, AA574155, AA576758, AA625711, AI274171, AV749543, AA583179, R56497, AW664258, AI400307, R56369, AA084546, AW248447, BF675036, AA805796, AI914573, AI183317, AA969588, AA516078, AA181067, AW192448, AA976451, AA961148, R56104, H22843, AI264478, N80562, AI263748, BE272880, AA352369, AW953396, AA325435, BF369001, RG2408, AA904367, AA211866, R62409, AA303270, BF095626, AA999773, AA917014, R38437, AW118274, AI150239, AA354306, H22844, AA355150, AA353139, BF799722, R80227, AA039646, AA321806, N40663, BG122562, AA321805, AJ364445, R12864, AA295363, AA641448, AW901335, AI001853, AI221522, AA303866, R49878, AW247358, T16973, BE206478, AW015905, AA180189, AA862561, AA743072, AA346787, R56274, AA343417, AA180499, AA279741, BE546075, AW007931, AW297178, AA179782, AI421063, R49877, AA279823, AI274516, BF796689, AI525802, AA095578, AW855537, AC003665.1, AC008550.4, AB051618.1, AA192915.
HFTDL56	212	695976	1 - 1825	15 - 1839	AW959215, AL514484, AU143560, AF307337.1, X55019.1, X01719.1, X04759.1, X01717. 1.
HFTDZ36	213	545726	1 - 1089	15 - 1103	AV721599, BF732420, BF510533, BF508158, BF508241, AJ638188, AW181935, AI758929, AW592730, BE967495, AA447514, AI078837, AV723652, AI218418, BF692673, AA884756, AI335250, AW118870, BE044339, AA426363, AV730822, AI868197, BF947599, AA927228, BF952754, BF952302, BF952504, AW905268, AW905266, BF952591, AI673798, BF952850, BF952505, AW905263, BF952750, BF952589, BF952851, BF952752, AA897687, BF572515, AW905328, BE699539, AI830527, BF952755, BF210822, AA431528, AA029326, H41714, AA437157, N53641, BE699547, AW905379, BE699537, BE796741, AW898982, AI218421, AF289076.2.

HFVAB79	214	130073 6	1 - 1161	15 - 1175	AC067967, 2. AI640273, AI769432, BF939574, AW271996, BE463585, AA916007, AI935583, BF196453, AI478387, AW301652, AI474065, N73883, W03943, AI266027, AI241273, AI373364, T87063, T83618, AC069548.4, AF349540. 1. BF362920, AI160269. 14.
HFVGE32	215	854545	1 - 558	15 - 572	AV648354, AV648120, AV719575, AV720522, AI207547, AI434618, AU145412, AV720302, BE463522, AI536648, AV718703, BE971199, AW772290, AV718420, AA705032, AV653985, AV648331, N68679, AV648215, AV648032, AW204828, AI276746, H55836, AV660303, AA995080, T88862, T72187, H55837, AV649505, T67491, AI521332, AC008014.5, AF305814.1, AK001053. 1.
HFVIC62	216	799525	1 - 1336	15 - 1350	AV699170, AV699125, AV699144, AV699136, AV662257, AW952432, AV662242, AV650031, AV662196, AV719825, AV719156, AV720062, AV720893, AV724349, AV699246, AV699147, AV724520, AV699197, AV699218, AV699247, AV662167, AV699119, AV699199, AV662268, AV662225, AV662149.
HFXAM76	217	601402	1 - 933	15 - 947	AV652810, AV699123, AW963961, AV662272, AV699182, AV699246, AV699223, AV699147, AV645788, AV699204.
HFXDJ75	218	626114	1 - 1904	15 - 1918	AV699204, AV699196, AV699199, AV725496, AW952432, AV652809, AW958904, AV662223, AV699218, AV719825, AV719156, AV720062, AV720893, AV648653.
HFXDN63	219	553685	1 - 1012	15 - 1026	BE736918, BE250577, BE616582, BE728115, BE615376, BE563291, BF793477, BG250960, BE386373, BF338817, BE531051, BF680445, BE385152, AU139668, BE883545, BG032917, AU120778, BF943073, BE899007, AW899342, BF803637, AV701925, AV706319, AU136531, AW957880, AW957801, AA307661, BF882363, BF217767, AA121877, AV732690, BF218444, BF203663, BE264980, BF957961, AI380547, AA134410, BF207674, BE061899, AA826146, AL133895, AA505043, BF733347, BE384186, AV730296, BE184422, H02956, AA583368, BE154390, AV742189, AA180023, AW276742, H92806, BF773043, BF815608, BF957954, AU116940, AA243106, BE304382, BF962070, BF811794, AA227286, AA715194, AA969742, AJ003034, AA221018, T60641, BF592342, AA179694, AV749263, BE565499, BE566249, AA584467, AA504672, BE736970, AI918674, T07838, BE792178, BF197329, AW630075, H47099, AW515786, BE968449, H78916, AW865469, BF951636, AA317928, AA503299, AW963317, AA782913, AI440300, AW899603, H67930, BF238662, AW899527, H63688, AW962826, AL134062, AA359714, H71269, AV750972, AA356190, AA572768, T92166, T60713, AA491404, AA431655, T57502, AV683302, AV698434, BF929662, H71280, BF67788, BE617381, T62188, AW898213, AV715734, AW865403, AW872342, AV682563, AW898920, AI088102, BF812273, AA173218, AW023095, BF920075, BE898175, AA984544, BF759180, AA601152, AV697443, H53927, R01106, BF873657, R24107, AA225638, BF911201, AA657747, T97032, T98711, AA74178, BE220229, AA081887, AA312997, AW864780, AI557831, AI142016, AA577789, BE884391, H67786, BF857863, W22010, BE165736, AU127460, N41805, AW855025, AW999271, AA281292, AA133041, AA083246, AA568139, AV731015, BF829537, BF874267, AA232145, BE564886, AA418919, AV731611, T97044, BF871285,
HFXGT26	220	745381	1 - 1743	15 - 1757	

AL940708, BF763808, AW997042, AL118813, AA353087, T59997, AA434462, BF869361, AW845664, AA833581, T94924, AW845678, AA431294, BE010787, AW845665, AV731929, AA614154, T57455, T63143, BF877837, BF869076, AV729748, AV691164, BE568189, W22978, BF212724, BF002494, BF675027, T70833, AW962273, AA136772, AC018641.3, AC006500.4, AC013470.10, AC005248.1, AL13321.11, AC084356.22, AC013357.19, AL161797.10, AC010745.4, AL133391.5, AC022415.5, AC008770.6, AL049555.6, AC015723.8, AL135796.6, AC016749.4, AL139109.14, AC066584.6, AC004711.1, AC011503.4, AP000827.4, AL358975.8, AC022325.5, AL049828.3, AL096862.18, AC007128.2, AL354942.10, AL391152.3, AC006027.1, AL109659.20, AC073964.3, AP002022.1, AL157367.15, AL022578.1, AL163268.2, AF051934.2, AC016748.3, Z92844.1, AC018645.4, AL139232.13, AL031655.8, AL157775.15, AC007320.3, AC007023.3, AL1359712.12, AL445590.4, AL022171.1, AC007221.2, AC015983.7, Z98046.1, AL161757.4, AL138961.17, AC003086.1, AL158153.10, AL354825.10, AC010148.13, AC019050.4, AC090954.1, AC024581.3, AL132985.4, AC010176.12, AC013751.6, AC007558.3, AC010634.5, AF279660.2, AL450169.1, AL031768.9, AL133153.3, AC008898.6, AC006355.3, AC012591.8, AC022443.4, AL022726.1, AL136441.16, AL136307.12, AL391478.14, AL139340.12, AL353741.16, AC007132.3, AC023795.18, AC073221.8, AC068323.8, AL139014.6, AC006203.1, AL162385.16, AL158093.8, AC006596.2, AC006385.3, AL357312.8, AF198097.1, AP001955.2, AC019155.4, AC010305.3, AL512428.13, AL078623.28, AL513264.8, AL163639.3, AL357092.4, AL161730.9, AC060232.5, AC004592.1, AL137000.6, AC002080.1, AC010143.3, AP001718.1, AP000194.1, AP000314.1, AL021877.1, AC002980.1, AC021017.4, AC006206.3, AC004053.1, AC025575.21, AL365367.10, AL445532.8, AL513128.11, AL356317.8, AL360020.15, AC008488.7, AL354802.15, AC004388.1, AL389889.11, AL355074.5, AC010722.2, AL513011.7, AL450345.6, AC016910.5, AP000742.4, AC004216.1, AC011594.8, AL360236.26, AC010585.6, AP000811.4, AB038490.1, AL158070.11, AC073308.4, AC020647.9, Z82195.1, AC002038.1, AC016711.9, AC007043.3, AL158206.8, AL022399.2, AC009301.3, AC006984.2, AC004000.1, AL356438.15, AC005344.1, AC008945.6, AC007313.3, AC000060.1, Z73986.1, AC027287.20, AL356601.14, AF280107.1, AC004056.1, AL109933.25, AC008551.5, AC009949.9, AJ277546.2, AC018741.3, AL162431.17, AC020644.6, AC069294.5, AC004694.1, AL157398.6, AC005798.10, AL118496.21, AF149774.1, AL358293.4, AC010104.3, Z98754.1, AC006002.1, AL118519.25, AC015522.6, AC018677.3, AC019041.8, AC073323.5, AC009623.6, AC018698.5, AC010348.4, AL1590788.8, AL445932.12, AC009517.5, Z83745.1, AC002066.1, AC005019.1, AL117375.12, AL096817.12, AC006257.1, AP001376.4, AC069285.8, AC006362.2, AL137145.13, AP001818.2, AL359502.14, AP002768.3, AF172277.1, AC008550.4, AC008277.4, AC007538.5, AL138694.18, AC005024.2, AP000647.4, AC005690.8, AC076972.16, AC010338.6, AL359755.9, AL121595.5, AL442646.14, AL117337.25, AC012492.9, AL590964.8, AC006568.7, AL391260.13, AP001002.4, AL031586.2, AL079307.7, AF225898.1, AC084783.2, AC005172.1, AC009779.18, AL356378.17, AC006479.2, AL008722.16, AC003977.1, AC005392.1, AC018360.16, AI391065.6, AC009264.6, AC009332.6, AI133319.24, AI353573.10, AI35834.1, AC008943.6

						AC074391.5, AC012442.7, AC024084.4, AP003467.2, AL096706.10, AL049792.11, AC006478.2, AC063956.7, AC046130.25, AL096704.8, AC021269.4, AL391867.5, AL353613.10, AC006371.2, AC009514. 2.
HFVG31	221	526253	1 - 738	15 - 752		AW002350, AV764465, BE158716, BF876961, AA724333, BE973589, AA812141, AW473455, T06754, AU159337, AA297769, AC005095.2, AL121869.19, AC007919.18, AC003954.1, AL161420.10, AL513264.8, AL035405.10, AC005038.5, AC016749.4, AC005548.1, AL031118.21, AC002553.1, AC004477.1, AL133545.10, AC008041.5, AC011422.2, AL353633.13, AC012005.4, AC005627.2, AL135841.11, AC027319.5, D14813.1, AC009137.6, AC034240.4, AC005884.1, AC034193.4, AL031848.11, AC009412.6, AC008125.9, AC018808. 4.
HFVHD88	222	589523	1 - 1588	15 - 1602		AP001741.1, Z49918.1, AP001610.1, AC009399. 5.
	223	609826	1 - 1859	15 - 1873		AI041718, AC006213.1, AC035150. 1.
	224	505207	1 - 927	15 - 941		AUI24431, AW960435, BF525944, AA781090, AW514159, AW390483, AW965129, AW170237, AW582015, AI700395, AI079309, AW339256, AI140441, BE700940, BE842726, BE842730, BE700936, BE700869, AW581975, AI022857, AI030397, AI401014, AI379419, BE700861, BE700862, BE772035, AI434349, BE772040, BE772042, AW673336, BE700873, BE700876, BE842723, BF439588, BE700941, BE700945, BE772099, BE700938, AA703354, N50989, BE772066, BE700937, AA719006, BE908235, BE772053, BE772081, H69547, BE700904, BE772059, AA574083, BE830929, BE772082, BE818955, BE818958, BE772101, AI251845, AI243536, BE772019, BF870875, BE818964, AW517983, BE700851, AI983670, BE772020, BF359589, H70004, AW820559, BE840628, BE700898, T63151, BG012510, R11344, AA305705, BE818962, BE840434, BE840457, AW752129, AA565124, BG010792, BF849721, BE772047, AI905362, AA731490, BE818915, BE772087, BE772018, BE772074, BF110884, R14845, BE772086, BE772015, AI983820, AA344670, AA889063, R07438, BE840445, C15468, T63006, BE170135, R09631, R06659, BE772017, BE836162, AI540442, BE830923, AI023272, AW868068, BE830919, AW868069, BE818892, AA324635, AW960971, BE818951, AW674579, BE832289, BF091071, AK001249.2, AB007936.1, AK027078.1, AL117402. 1.
HFVKT05	225	658690	1 - 1701	15 - 1715		AA483223, AA552843, AV762050, BF991286, AA623002, BF827410, AW193265, AI434706, AV759204, BE350475, AI270117, AV760937, BF217299, AV710066, AA610493, AI350211, AL041690, BF475381, AV764241, AV764307, AW673241, AV762139, AI192631, AA552856, AV763540, BF676536, AA468131, AV682003, AI368256, AI345157, AA649705, AI345518, AV760774, AA480772, AA521323, AI538433, AA644538, AL037683, AA577906, AA613227, AA503475, AW270382, AI355206, AW021583, AV759274, AA521399, AV761155, AA492166, AV735495, AI431303, AA490183, AW088846, AF330238, AA857486, AA493621, AV759382, AW438643, AA579362, AI610159, AA525790, AA507824, AV742057, AV763255, W60061, AV761786, AA644551, AI254615, AV735370, AW872676, AA649642, AA652057, AA984708, AA579736, AA682912, AA525824, AW238583, AW977303, AA470969, AI963720, AV734666, AV760624, AV762826, AA970213, AA908422, AI613280, BG150790, AV760777, AA834755,
HFVY27	226	634161	1 - 931	15 - 945		

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HGBFO79	227	422794	1 - 1524	15 - 1538	AL529939, AL529940, AL528803, BE735106, BE798231, BE745759, BF312738, BE877016, BF343676, BE727149, BE549483, BE902824, BE903952, AL045805, BF310548, BE735699, BG259719, BE909739, BG030614, AW151250, BE382644, BE293088, BE907275, BE902845, BE390391, BE617060, BE886529, BE888201, BE313296, BE897351, BG253429, BE515066.

AW732704, BF791531, BE409147, AA402631, AV708863, AA502644, AA724973, AA057574, AW957597, AV702553, BF973113, BG180500, AV702396, BE742746, AF755278, AA290638, BE903995, AI089475, AA887805, AI161001, BE392156, AI342640, BF245183, AF820884, AL079399, AA993506, BG105105, BE019281, AV723744, C06428, AI310732, BE904398, BE378151, AA676716, BF980925, AA402669, AA558203, W46517, BF155847, AA324688, BE794205, AA682577, AI086193, AA350920, AA410238, AA436330, AA430533, AW863222, AA477605, AA355049, W52276, BF972686, R98071, BE741396, AA430492, AI659749, BF089390, F31374, BF984040, BE909563, BF357217, BF357202, H54089, R84453, BE794934, R54514, BF357191, BF357182, BE544952, BE091550, AA329392, AA203205, W88866, BE799599, F05766, AI528802, R76898, AI828302, AI909292, R79667, U46298, U46408, AI783909, AA290651, BG027789, AA325152, R77063, AA419293, AA284571, W03246, AA433853, BE379015, AA344489, BF812320, BF993643, AI207133, T74861, AA477478, BF083007, AA776079, BF806431, BF806761, AA687586, BE074631, R79856, BE769336, H80942, BE769313, T93671, BE769337, AA432307, W47495, BF243313, BF332596, AA326252, BE769318, AW840219, N43759, BG007721, BE934503, BF360558, AI909265, F36499, AW899414, BE699889, AV735591, BF345660, W40292, AA960832, BE094772, BE645528, AI912787, BE769393, AI909264, N83578, AW899503, BE774020, BE699857, AA977993, AI656270, AI631977, BE138644, BG179295, AI859644, AW089006, AI349957, AI345005, AI635164, AI873638, AW193467, AW089275, AI348917, AI865289, AI345014, AI537837, AW411298, BE393551, AI916419, AI560096, BE875959, AI933992, BE872082, AA127565, AI345261, AW059713, AW411351, AA806719, AI336633, AI583578, AW023590, AW189301, AI345677, AI633061, AI340627, AI573026, AW409775, AW168503, AI590423, AI491904, AW083572, AI918554, AI344931, AL038575, AI470714, AI537643, AI582871, AI281772, AW302992, AA468418, AW074869, AI432570, AW083168, AA983883, AI863047, AI453199, AI929108, AA853213, AA853539, AW081383, AI348870, AI561356, AI631216, AL036652, AA494167, AI951516, AI355277, AI565172, AW366372, AW827203, AW152369, BC000655.1, BC009265.1, AC002094.1, AL110156.1, BC001655.1, AK025375.1, BC000348.1, BC008780.1, AL049466.1, AK027102.1, AK026542.1, AB055370.1, BC009311.1, AB055805.1, S77771.1, AL080140.1, BC009395.1, BC002355.1, BC004119.1, AF094850.1, BC001093.1, BC007198.1, BC008364.1, BC008938.1, BC000090.1, AL389935.1, AL136979.16, BC004883.1, AK025209.1, BC003587.1, BC002409.1, AL136845.1, BC008417.1, S76508.1, AF242525.1, AL133640.1, AF120268.1, AL117578.1, BC004333.1, BC008282.1, BC005678.1, AF104032.1, AL137476.1, AK026591.1, AF090943.1, BC007456.1, AK027182.1, BC008078.1, AL162085.1, AF146568.1, AL110224.1, AF207829.1, BC007375.1, AF276658.1, BC006480.1, BC001967.1, BC004362.1, AL080126.1, BC004310.1, AK024622.1, AB051158.1, AF218014.1, AK026626.1, AL136844.1, AB063093.1, AJ010277.1, AL050138.1, AL137521.1, AL359624.1, BC009403.1, BC001774.1, BC008070.1, AF218031.1, AB049629.1, AK024974.1, AB048974.1, AL137554.1, BC001098.1, BC003101.1, BC001206.1, BC001470.1,					
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HGBHE57	228	566836	1 - 649	15 - 663	BF591002, AI491940, AI239822, BF440034, N20580, AI263983, AA526882, AI811694, AJ080116, AA046053, AA902625, AI536055, AI361914, AA622321, AI421561, AA508633, AW661932, D20772, AW952992, N67184, AA526869, AI598052, H64253, AA282273, BE618852, AA811240, AA345238, AW732176, H17050, AI061405, H23158, BF592162, T80830, H09571, R53226, AA046179, BF759956, H25064, T86412, BE890120, H09750, H21812, AW379527, AA249340, AL514791, AL514473, AI863382, AL513817, AL513991, AL514511, AI499178, AA765198, AI401697, AI434731, AI863002, AI440238, AL121286, BG163646, BG117249, AW196720, AW955902, AL039287, AL513693, BE965000, AI564212, AI971587, AW051088, BE883591, AL513977, BE966443, W45039, AI619820, AW088717, BF793561, AI696714, AI491842, AI890887, AI421662, AI471429, AI479292, AW021464, AW087217, AI925502, AI524654, AI961631, AL037104, AI250821, AI453767, BG108070, T69241, BE910033, AI439962, AI434468, AW090736, AI568967, AI432532, AI251221, BG119855, AI478714, AI784214, AI553645, AI470717, AI690813, AW194014, AW128971, AW105431, AI435641,

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HGBIB74	229	837220	1 - 1802	15 - 1816	<p>AU132073, AL514534, BF983632, AL526111, BF793202, BF816636, AL526167, BF207035, AU121857, BE312932, BF307465, AL528311, BF316637, BE878180, BF512924, BE781366, BE299008, BE866833, AU141579, BF307539, BE296624, BF203318, BE314690, BE247312, AA258714, BF203434, AA258479, AW602250, AW372226, BF358908, AA625114, A1337232, BF762063, AU134960, BF303835, AW372227, AU125523, BE840047, A1739102, BE696707, AA551238, AA505288, R52096, BE746044, AA853934, BG012508, A1936957, A1582908, BE245999, R46499, BF365473, BE296121, AW166753, AA770298, BG056533, AA481002, AW071542, H17104, AW007814, A1086723, A1338746, A1340064, A1094613, A1096869, A1922132, BF939399, BE855621, A1357394, A1423481, AW087313, BF475441, A1421759, A1356823, A1418892, AA287330, N94480, AA524286, AW005778, A1922862, AW191028, A1566341, AA470698, A1421557, A1361016, A1359797, A1362874, A1863909, A1880712, F09352, A1922424, AA873767, AA481480, BF447091, AA291405, N20109, A1263664, AW968514, AA570059, A1913894, BF057036, W94068, BF090405,</p>

					<p>AI381877, AI193950, AI364237, D54296, AU149162, BE828094, BF751874, AA789159, AA853935, AA482101, AI360188, AW952710, ZA0719, AA400811, AI539565, AA629142, BE813293, AA095376, TS8139, AU147592, AI214242, AI034063, N31573, AI040574, H43298, BF753185, AA953460, AW131152, AV706318, AI146352, AI648405, AA921717, AW054979, AI445988, AI888216, BF432411, AI271977, R22588, AI360977, AW188664, AW516744, AI085523, AW057831, AI613427, AA679957, AA524336, AW993553, AW375413, M79269, AI598125, BF819300, AW993667, AI083784, H65453, AW136876, BE964668, AA421021, F30056, AL515965, AI078721, AL515964, BG060060, AA701072, BF805411, BE815632, BF872254, BF752405, BF527514, W94067, BE762789, W23927, BF206436, BF527026, W22794, BF72933, AW265783, BE707365, AA480986, BE259841, BE876343, BE697298, D87444.1, AL049539. 21.</p>
HGLAL82	230	520261	1 - 392	15 - 406	AL117344.12.
HHAAF20	231	838603	1 - 1481	15 - 1495	<p>BE562242, BE782638, BE542785, BE871376, AW962260, AW118853, BG163298, AU151024, AW956135, BG254474, AI014552, AU153853, AI128005, AI304951, AU151709, AU123132, AI806634, AI554797, AA864943, AU151959, AW956137, AW731743, AI023423, BG150021, AI859224, AA001739, BF725954, N51229, BF476487, AI206406, AI422749, AI888568, AW511373, AW966806, BF110112, AA776417, AW192477, BG027748, AI161044, BF913352, AI306577, AA878001, W37987, AA587858, AW072232, AW451522, T57196, W37988, AA477029, T94775, AA022682, N24284, N32175, BE696738, BE857520, AI022374, AA527439, AA282898, AI538443, BE703950, AI208820, T55949, AA022801, W79912, W02715, BE041622, AI420754, AA911458, AA813028, H80241, W78127, BE221072, AU156435, AA884339, AA309975, AI276411, W03712, AA321763, W27545, BF887745, AA548566, AA339184, W25734, T94024, AA370906, AA001808, AW020249, H56404, BF926153, AI499535, AI869412, R22900, AI828446, BE241440, BE243664, AJ293456, AI146581, R23002, H56188, AI824776, AA321910, M85881, C01054, AA872708, BG166236, BF942843, BE541266, BE158250, AA971014, AI243389, BC000978.2, AK022524.1, L39210.1, AK000266.1, L33842.1, AK025013. 1.</p>
HHBCS39	232	100302 8	1 - 2881	15 - 2895	<p>AU118319, AU118145, AA001321, AI268416, AU144910, AA004368, AW291988, AU144790, AA677418, AI056605, BE708494, AA001908, AA707413, AA903931, AA004369, AA122399, BG000061, AI152481, AA878867, AV695708, AA152372, AI279749, R28072, AI446406, AI565299, T82947, R28288, AA346924, T97751, T97858, AI242583, AW839578, AK024922.1, AK021612. 1.</p>
HHHEA08	233	638231	1 - 2136	15 - 2150	<p>AL520596, AI370425, BE567612, AI343143, AI016704, BF678494, AI284640, AI952900, AL038606, AW302048, AI049996, AW500125, AA318267, BE139267, AW979140, AA484143, AV763401, AW021774, AI345123, AW302315, AI754661, BF725347, AV762129, AL039187, AL079734, AI344810, AV763657, BE676900, BE139358, AI045077, AA192278, AW069227, AV710066, AV758989, AL526288, AA528480, AW303196, AW088125, AI270117, AA491814, AW301350, AA448838, AI538812, AL041706, AI918013, AV682003, AI754291, AU154948, AV760937, AW419262, AV728928, AW833862, AW731867, AW238016, BG031290, AI696793, AA524832, AA601680, BF926429, BF916934, AI473701, F32710, N91310, AA730635, AI634187, AW193265,</p>

AW504224, BG033217, AA167055, N22032, AV755512, AL046409, AC016601.6, AL121988.10, AC010219.4, AF235097.1, AL035450.1, AL132986.4, AL133260.12, AC004000.1, AC005291.1, AL031431.8, AC009087.4, AF130343.1, AL138880.14, AC007036.3, AL132987.4, AL031719.12, M69197.1, AE006467.1, Z85996.1, AC012076.4, AL035400.13, AC007564.9, AC006206.3, AL449212.1, AL158830.17, AL356378.17, AL049569.13, AL031584.1, L78810.1, AL121845.20, AC007566.2, AC011465.4, AC005540.4, AC025572.13, AP001713.1, AC002352.1, AC007193.1, AL139092.12, AF001549.1, AL121865.7, AC010458.5, AL121895.26, AL133415.12, AL121657.2, AL389921.12, AP000100.1, AL031727.42, AL161747.5, AC008395.6, AL353140.12, AC073593.13, AL157828.14, AL157398.6, AC079141.7, AC006952.6, AL034431.16, AC078962.30, AC008882.6, AC009228.4, AP001694.1, AL121899.37, AC005697.1, AL160273.9, AL031291.3, AC008745.6, AL137859.3, AL161896.16, AC007055.3, AL121910.26, AL117328.5, AL450169.1, AC005768.17, AP000208.1, AP000130.1, AC005071.2, D83989.1, AP002008.5, AP000247.1, AL353613.10, U95740.1, AC002045.1, AC006057.5, AC009314.4, AC008747.5, AF279660.2, AC004231.1, AC078961.23, AP001725.1, AL035089.21, AP003357.2, A003147.1, AL359739.8, AL352984.4, M55538.2, AC005304.1, AC079045.2, AC004522.1, AF241728.1, AC007221.2, AL161937.13, Z82097.1, AF069291.1, AL110114.1, AC008482.5, AL109615.41, AL391122.9, AC018618.5, AL161421.11, AL049869.6, AC010489.4, AC005007.1, AC083870.2, AC006285.11, AL158035.14, AC007198.6, AC078876.15, AF243527.1, AL391280.15, AL031681.16, AC016025.12, AL160410.24, AL138762.20, U93305.1, AL031985.10, AL121754.18, AC008394.3, AC007161.1, AL590732.7, AC022212.4, AP002851.2, AL356321.9, AL008708.4, AL359846.11, AC006270.1, AL050349.27, AL445483.13, AC005325.1, AL353748.13, AC009955.4, AC002381.1, AL122004.17, AC009230.3, AL049776.3, AP001710.1, AC008547.5, AC008555.5, AC005520.2, AC002565.1, AL031176.8, AL138741.13, AC005678.1, AC004590.1, AL133551.13, AC009238.4, AC007673.7, AC008872.5, A7289880.1, AL096793.20, Z85987.13, U57009.1, AC004890.2, AC005822.1, AL590762.1, AL160237.4, AL391684.6, U91326.1, AC083875.1, U96629.1, AP000426.3, AC013429.12, Z98051.6, AL031055.1, AL049758.11, AC004826.3, AL355096.4, AC009309.4, AP001830.4, AC008755.6, AC007749.3, AC005887.3, AC002395.1, AC002418.1, AC010504.7, AL161627.13, AL118511.25, AL139317.5, AL442203.12, AC004386.1, AP001972.4, AC016830.5, AC004832.3, AP001614.1, AC004846.2, AL035685.21, AC005701.1, AL132713.11, AC007465.4, AC005669.1, AL352976.3, AF134726.1, AC006052.5, AL133328.13, AC079684.16, AC011739.7, AC016027.15, AL359851.19, AC078958.30, AC022173.7, AC011359.5, AC006026.2, U57007.1, AL139100.9, AL445675.9, AL445258.4, AC009470.4, AL133324.13, Z82194.1, U18391.1, AC002316.1, U18394.1, AL356801.5, X54176.1, AP001781.4, AL135907.21, AL353734.12, AL031963.40, AL133338.8, AL135744.4, AL121601.13, AL359813.23, AP000036.1, AC009464.7, AC004812.1, AC018710.4, AL160192.3, AC026463.4, AL109825.23, AL121902.13, AC019041.8, AC079602.15, AV726528, BF574791, BF996057, BF990910, BF035428, BF695329, AI096792, AW977965, AA811457, AI742527, AI820061, AI921596, AI984225, AW961815, AI393746, AI573202, BF970504,	15 - 3102	1 - 3088	823100	234	HHM/A59
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HHHMA75	235	494099	1 - 851	15 - 865	<p>AA464839, BE269516, AW470830, AI808512, BE907567, BF381742, AW044532, W20358, AA780196, BE894120, AA450310, BG115487, BE767266, AW504536, AA243525, BF248139, AI218646, AI358214, AC008154.6, AC018646.3, AK027726. 1.</p>
HHHMM74	236	941955	1 - 2598	15 - 2612	<p>AI912020, AI738591, AL530623, BF000400, AI673200, AW195629, BF590333, BE465055, BF342074, AW207103, AI914327, AI016102, AI948562, AA515654, AI858984, AI021976, AA824295, AW003109, BG106995, AI288261, AI332790, AW873004, AA447206, AI863407, AW271426, BF222197, AI673222, AW274813, AI093417, AW197033, AA846300, AI989749, AA917651, AI933079, AI198249, AA149282, AW337461, AA029228, AU120416, N89854, AA476264, AI650694, AV760466, AA805734, Z28929, AV762395, AI042753, AI862408, AW137892, AW250017, AV759518, BE744242, AL138435, AV762645, AW582878, H43959, AI679782, AA029227, AL043009, BF337291, AA078301, AV682003, AV763971, AV720371, AI400383, AL042853, AL138265, AI971136, BG116267, BG116323, BE874842, AL043718, AV733824, AL079812, AI284640, AW954829, AI133164, AF039185, BG249643, AW301350, AV762098, AI805607, AW303196, AI334443, AV763633, AI499938, H01583, AL037683, H01483, BF677892, AL041690, AV760391, AF330238, AA587604, AL046409, BE893169, AW274349, BF241967, AL048626, AL045053, AV761745, AA631507, AL040921, AI963720, BG116150, AV761362, BF690726, AV760389, AV764530, AI307608, AV763540, AL119691, BF668217, AV759704, BF676981, AV759204, AV762959, AU140493, AU147104, AI431303, BF680074, AA581903, AI270117, AW812477, AW965008, AV710066, AW021583, AW088846, BG059568, AW072923, AW193265, AV728425, AA610491, AW419262, AW518220, AI613280, BF475381, AA129446, AV760777, AA594725, AV725423, AV762139, AV760937, BE562953, AA723017, AL039996, AI254316, AI281881, AL042377, AW576391, AI350211, AW995093, AW502975, AW574794, AW188484, AV763354, BF311000, AV733830, AU118745, AA490183, AI708009, AI610920, BF697673, AI862409, AA563926, AV757607, AV735495, AI305766, AA584082, AW406447, AI192631, AV740801, AL046205, AW270270, AV742057, AI367497, AI537506, AV762050, AV761489, AW245747, AI457397, AA577906, AV764329, BE252421, AI076616, BF792268, BF965232, BF965007, AW276827, AU152722, AW265385, AI343654, AW662543, AW969629, AI097429, AL134972, AI754955, AV756220, AI821271, AI537955, AW501386, AV658688, BF918590, AL120687, BE150580, AI924251, AV735370, AV763255, AV764228, BG236735, AV762111, AL044940, AV764578, AI732865, AW960468, AW974109, AI370074, AA547979, AI625244,</p>

AV764398, AW276586, BF919090, AC004084.1, AK025420.1, AK026441.1, AB011110.2, AC008569.6, AC005696.1, AC009996.7, AP001717.1, AL160269.14, AC008372.6, AL355543.13, AC009756.9, AC009412.6, AL139317.5, AC000025.2, AC005015.2, AC005077.5, AL132768.15, AC009516.19, Z85986.1, AF053356.1, AC006329.5, AP001695.1, AC006480.3, AC007318.4, AL359091.10, AC004963.2, AL023284.1, AC011497.6, AC004686.1, AL138724.12, AC011495.6, AC068724.7, AC012476.8, AF196779.1, AC005081.3, AC008610.6, AL139415.10, AP003357.2, AL022721.1, L44140.1, AL035367.5, AC010789.9, AC012170.6, AC010319.7, AP001688.1, AL163249.2, AL139330.17, AJ003147.1, AC021016.4, AC020904.6, AC005839.1, AC004166.12, AC007055.3, AL353807.18, AL161747.5, AC008543.7, AC004089.25, AC010326.6, AC011811.42, Z93017.6, AC004832.3, AC004638.1, AC019205.4, AL133367.4, AL133477.16, AL049759.10, AC011475.6, AL354707.17, AC002350.1, AC005695.1, AJ300188.1, AC009220.10, AC005291.1, AC005821.1, AC025594.5, AP001670.1, AC005037.2, AC005670.1, AL118520.26, AC004019.20, AC011442.5, AC009228.4, AC006285.11, AC005520.2, Z99716.4, AL117381.32, AC020906.6, AL356299.16, U91326.1, AC002565.1, AJ400877.1, AL109804.41, AC068533.7, AC009144.5, AC005940.3, AC022211.5, AL133284.13, AC009137.6, AC006241.1, AC006965.3, AF131216.1, AF334404.1, AC003037.1, AC008280.4, AC008403.6, AC008481.7, AC008567.4, AC006449.19, AL121601.13, AL133174.15, AJ312686.1, AC026464.6, AP001725.1, AL583856.6, AC044797.5, AL135839.15, Z97054.1, AP001714.1, AL035587.5, AC022150.5, AL096840.25, AC007193.1, AL162231.20, AC002316.1, AC008760.6, AL445686.14, AC007227.3, AC006435.7, AC006960.1, AC005052.2, AL160471.5, AL034380.26, AE006463.1, AC024028.10, AL096841.6, AC008812.7, AC025262.27, AL121890.34, AL049776.3, AL022163.1, AC006211.1, AC078878.20, AL136137.15, AC007991.7, AC005527.3, AL035458.35, AC005837.1, AP001748.1, AP001671.1, AL590763.1, AC007546.5, AP001753.1, AL590762.1, AL135927.14, AL158830.17, AC016025.12, AL022238.1, AL030335.32, AL121972.17, AL031283.26, AC008491.6, AC008481.19, AC069548.4, AC005231.2, AL161656.20, AL445222.9, AL049795.20, AL135901.23, AC004453.1, AL109935.39, U95742.1, AC005620.1, AC007298.17, AL352978.6, AL109797.18, AL356915.19, AL162426.20, AL139809.16, AC011487.5, AL023553.5, AC067941.7, AF129756.1, U80017.1, AC004821.3, AC010458.5, AL354720.14, AL096701.14, Z69666.1, AL031587.3, AC002549.1, AC026172.3, AC011816.17, AC004840.3, AC011448.3, AC010271.6, AL133485.3, AL133448.4, AL160237.4, AC011479.6, AC005488.2, AC022596.9, AC007666.12, AC006483.3, AC006512.12, AC008519.4, AC007005.3, Z83844.5, AC084864.2, AC005778.1, AL133551.13, AC005971.5, AL020993.1, AL121891.22, AL391827.18, AC027125.4, AC025593.5, AC005295.1, AC024561.4, AC012306.11, AL096776.12, AL157372.18, AB038653.1, AC006251.3, AC018644.6, AC005086.2, AC018808.4, AL033521.2, AC005562.1, AC004867.5, AF001549.1, AC004965.2, AC005519.3, AC007676.19, AC008115.3, AL513008.14, AC009263.6, AL136418.4, AL139054.1, AC000360.35, U62293.1, AC010378.6, AC027644. 9.				
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HHENQ22	237	589958	1 - 1885	15 - 1899	
HHEPD24	238	498227	1 - 224	15 - 238	
HHPEM33	239	877639	1 - 1445	15 - 1459	<p>AI525047, BE267465, AU119027, BE728398, AU142237, BG034269, BE797542, BG110205, AI525046, BF446035, AW966408, BE695857, AA447885, BE261226, BF852227, BE858413, AU159593, AV749929, BG178599, BE856576, AA424770, AI338990, AW135009, AI423774, AI334334, AW959286, AI766429, AA417903, AA933079, AA424903, AL047160, AI685395, BF477465, AW139987, BF948688, BF745006, AW769824, AA641849, AW371401, AW371406, BF745011, AW613024, BG056135, BF744933, BG058480, AI720305, BF744994, BE828620, BF744932, BF744930, AI250926, BF760364, AA593807, AI969741, AI263347, BF744931, BF745007, AA383851, AA482522, BF745014, AI686024, AA447724, AW613546, AW614328, AI766856, BF995409, BF745010, AA644474, AW197307, AA641850, BF852819, AA383850, AA325769, BF955849, AK023968. 1.</p>
HHPT60	240	463027	1 - 518	15 - 532	<p>AW135036, BG231414, AV743105, AI420838, AA535125, R16804, AI497603, AA813296, AA552195, BG236687, BG231242, AA504055, AA533150, BF971602, AA143324, BE907116, BF971381, AI475621, AW975063, AV760867, BF026034, AV710618, AA578143, BF306800, AV716075, BE881501, BE888689, AA729466, AA628531, AA482870, BF527622, AV662287, AV761533, AI582791, AI741580, AV701482, AV739097, BE257844, AW083024, AW203954, AA523344, AA532593, AV756558, AI497618, AW958877, AV762499, AA558231, BG059296, AI475653, BG231063, BG231145, AA514368, AI524728, AV738333, BF340078, AI589583, AV762734, AV703106, AW955488, AV737930, AV717668, AV755789, AV762182, AV755769, AV701025, AV762924, AC010451.7, AC016993.4, AC018684. 3.</p>
HHPEU04	241	838217	1 - 1070	15 - 1084	<p>BG034488, BF982559, BE794497, BE313144, BF314688, BG120997, BE910635, BF969005, BF340441, BF306972, BF525733, BE875593, BG030710, BF792430, BE262728, BF315735, BE314135, BF205034, BE276651, BF203164, BE387269, BE266232, BE391657, BF204545, BG027046, AA643840, BE260130, N63475, BF195525, AA205661, AI832232, BF058723, AI869318, W72049, BE018923, AI765058, AV687411, AA034035, AA553820, AW961121, BF304202, AI808064, AW026472, AI955852, AI765242, AW248507, BE393296, AI127262, AI277854, AI884693, AI073710, AW872762, AI376148, AA146971, AI765029, AI339947, AW024138, AI147240, BF061732, AA708126, AA813521, AW439832, AI694928, AW242703, AI498928, AI123913, AA836303, BG222313, AA156956, AI301956, AI347608, AI311112, AI268993, AI304651, BF435947, AI075899, AI560747, BE295615, AI346935, BE669425, BF195494, AW839917, W79426, AV687766, AA781466, AI342962, AA033915, AW136724, AI090370, AA625788, AW800090, AA709462, AI338271, AW079287, R47883, AI969210, AA399114, AA041385, W46277, H99183, AA770182, H94295, AW404352, AA741397, N23743, AA044694, N24466, AA974145, AV683814, BF889167, AA156864, AA398056, N40747, N35718, N94773, AW968213, AA146970, N30038, BE140096, AA468399, AI341986, AA708782, AI686517, AA704970, AI597845, AI038344, W76401, AI374736, H81310, AI497678, N32448, AW204374, AA868201, BG152852, AI291572, AA478165, AA468439, AA478010.</p>

<p> AI423158, AA707176, H81366, AI219428, R47882, AA127044, W95282, AA298982, BE928658, AI203479, N36015, AW243034, AA041191, W94777, AA993215, H94190, AV661716, AV708035, AA704288, AA991336, AA745913, AW204258, N59833, BF081714, AA025410, R06215, AI357603, AA298843, AA513969, AI379942, AI357554, AW000874, AA125766, BE645626, F27351, AA935742, BE833225, H45882, AA542901, AA564888, W79326, AA296786, AA564958, AA970265, AI761938, F30350, AI762149, AA041429, AI220792, AI869708, AA297517, AW188811, BE312203, AI919010, AW235465, AW090329, AA298624, AA298368, BF591489, AI956005, AA041425, AA298370, BF311814, AI749204, AI867544, AA296693, N44247, AI887211, AA045652, AI369692, AI365332, AA029123, AI566992, AV687884, AA918262, AA846379, AI269986, R36822, AI915437, AA297475, AV687881, BE090937, BF889173, F30226, AA205774, N76364, T24460, BF750936, BE066853, AI345416, AI345612, AI345415, AI251221, AL039086, AI345010, AI307569, AV739365, AL036509, AI349957, AI345005, AV743129, AI345688, BE138658, AI345608, AI340511, AI345471, AI348901, AV736808, AI345739, BC002911.1, BC000828.1, BC000215.1, AB063079.1, BC006119.1, AF112208.1, BC004265.1, AL512719.1, AB055366.1, AF132676.1, BC006458.1, AF061836.1, AL110218.1, AL136767.1, AF230402.1, AC002467.1, AL1389935.1, BC007534.1, BC007920.1, BC004899.1, AL137529.1, AL137480.1, AL359620.1, AF217982.1, AK000421.1, S77771.1, AL133640.1, BC001045.1, AB060226.1, BC008037.1, BC005843.1, BC001778.1, AL161953.1, BC008282.1, BC002370.1, AL050138.1, AK026534.1, BC000632.1, BC008899.1, BC003587.1, AK026959.1, AL096751.1, AB060229.1, BC008382.1, AF090934.1, AK024588.1, BC005805.1, BC001128.1, U55017.1, X67688.1, AL133075.1, BC004131.1, AK025015.1, AB063087.1, AF069506.1, AB044547.1, AL359623.1, AL136615.1, BC005168.1, AK027173.1, BC007241.1, AB048974.1, BC003602.1, BC001675.1, AL133049.1, AK024570.1, AF225424.1, BC001215.1, AK027213.1, AK000310.1, BC001056.1, AJ296345.1, AL137284.1, AL137547.1, AK026857.1, AL137478.1, BC006481.1, AL137459.1, AK026613.1, AB063088.1, AK025465.1, BC002491.1, AF003737.1, AB050411.1, BC002809.1, AB050533.1, AB060903.1, AL110221.1, AL389939.1, S76508.1, BC004943.1, AK026647.1, AF094850.1, AL133067.1, AL157480.1, AL049283.1, BC004370.1, BC004924.1, AL117457.1, AL157431.1, BC007732.1, U95738.1, AK026600.1, BC005002.1, BC008185.1, AL162002.1, AK024524.1, BC009026.1, AF358829.1, BC008649.1, AL050277.1, BC008488.1, BC007255.1, AB047941.1, Z82022.1, AK000655.1, AK026452.1, AF321617.1, AL133112.1, BC008708.1, BC004960.1, AL137627.1, BC008920.1, BC001294.1, BC003651.1, AK026504.1, AK024533.1, AK026480.1, BC002839.1, AL110196.1, BC003614.1, BC008836.1, BC006164.1, AL357195.1, AB056421.1, AB055328.1, AK025092.1, AL512746.1, AL390139.1, Z37987.1, BC002356.1, AB060888.1, AL137256.1, BC000054.1, AF352728.1, AL034400.2, AL136766.1, AF230496.1, AL137292.1, AL157433.1, BC006195.1, AL080118.1, AL512883.5, BC009285.1, BC008364.1, AK027095.1, AB060883.1, X6S873.1, AL136784.1, AL133061.1, AF260566.1, AL080126.1, BC005872.1, BC005021.1, AL137538.1, BC000090.1, AB060852.1, AK000618.1, AL137521.1, BC008417.1, S78214.1, AK026593.1, </p>				
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HHFBY53	242	821330	1 - 856	15 - 870	AA346699, BE897269, BG109478, BG178294, AI370129, AW238611, BF343729, AI000070, AI085870, BG179993, AI436456, BG108324, AV755207, AL514935, BE047863, AI802542, AI349772, AI500077, AL513643, AL121270, AI524684, BG165209, AL036396, AI225230, BF725126, BG260037, AI250293, BF883916, AL047042, BF343172, AW303152, AV655645, AL119049, AL036802, AL513907, BE048081, AL514627, AV681857, AW827203, AI064830, BG036846, AL046849, AI702406, AI475371, BF037097, BE048071, BE969709, BF727212, AV757737, BG111647, AL135661, AI521012, AI675423, AI433157, AL515041, BF971016, BF054877, BG168696, AW268253, AL121365, AL513597, AW075351, BE964812, AV682479, AL119791, AV681716, AL036146, AV756770, AV710479, AV757943, AI349645, AV711924, AW827249, AL119748, AV682224, AI187180, AI216146, AV681647, BG151247, BG031815, AV682266, BF969494, AV704928, AW238730, AV762488, AV682330, AL513911, BE968552, AL513837, BE887488, AI568870, BE613622, AV717179, AW274192, AI340582, AI687728, BG058208, AV721967, BF724691, AL514919, AV682351, AL513693, AI815383, AW071349, AW301409, AI349933, AI868831, AV682249, AI538716, BE966388, BG259801, AI349004, AI433976, AL045500, BG109125, BF795712, BF968493, AI687376, AV733470, AW071417, AW089572, BE880190, BG257535, AI799199, BF812933, BE964700, BG180996, AI969567, AI440426, BG114104, AL047763, AW074993, AI567351, BE048179, AV755290, AI281779, AV759235, AV757158, AL513553, AW195957, AI686926, AI678302, AI312152, BG252929, BG110797, BF695032, AV682074, AV681548, AV733397, BE877769, AA494113, AI687415, AI349937, BE785905, BF726421, AI497733, AW827211, BE965556, AV681685, AA610426, AW103371, BE048026, AI631107, AV757012, AV734318, AW169653, BE777769, AI345735, AV682441, AV758110, BG250190, BE876033, BG178809, AI699857, AL513753, AI635461, BF792099, BE048163, AI439087, AW162071, BE018711, AV755581, AL120854, BF793644, AV757018, AV723953, AI590128, AL513803, AV757853, AI275175, AV705644, AV758592, BE048319, BE047952, BG029399, BF970162, BE881155, AL514791, AV681630, AV758217, AW068845, AI863014, AI564719, AV682252, BG109270, BG108147, AL036274, AV757797, BE963035, AI934036, AI620284,

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HHFEC49	243	905849	1 - 2249	15 - 2263		W72062, AI827219, AI631461, W76255, AW449295, BF848562, BF849620, AI354957, AI222040, AI913803, T62772, T62921, T63781, AA364800, AF088057.1.
HHFFJ48	244	634521	1 - 2552	15 - 2566		BF872051, BF760479, AA486028, AL536141, N91095, AW301931, BF772459, AW852705, AW852684, AW852657, BE138714, AB058744.1, AL589723.7, AC006512.12, AL451107.6, U47924.1, AL590762.1.
HHFGR93	245	865581	1 - 1821	15 - 1835		AL513572, AL537139, BE869616, AL513571, AW190823, BE868295, BF528807, AW959200, BF998261, BF986378, W52782, BG009530, AA707399, AI921717, BE161072, AL656071, AI809901, AI870870, AA780017, AA046658, AA913618, AI633244, BF995431, AA428298, AI014541, AW300019, AW173046, AA428713, H12307, BF432551, H12782, BF115565, AI141481, AI092488, BE550395, W58612, AW172540, AI184646, BF222972, W58613, AI359381, AW361707, BE043092, AI970137, AI126255, R77354, AI624748, AI949837, AW081182, AI923177, AI187105, BE707255, R69232, AA514466, BF995428, AI521359, R69114, BG011026, AI347221, R76149, R73827, AA664044, R79810, H12841, AW594241, R78260, BG015155, BG002356, BF851373, H12629, R76098, R32862, R63063, R78261, T47327, AI189377, R73853, R62315, R68433, AI828342, R79923, H12360, AA618505, H12680, T50332, R79910, AW903922, AA733001, R35438, AI216465, AW903849, T98690, R73852, R81664, H00855, AA683601, AW009057, AI873711, AW513081, R33685, H02334, AI189455, AW365832, H02440, R67936, H02804, AI569353, R66838, R68432, H38189, R76065, R64387, R75889, R33581, R35749, AW235425, BG055882, R27675, T98640, AA991630, BF196820, AI189443, BF848636, R81467, BG007447, AA367816, R27576, R63218, R31360, AA359117, R31889, R34252, AI762218, AW002259, BF848635, W52486, H01235, AI199859, R62314, AA046788, AA249358, R64386, AW407088, N55686, R67441, AA446485, D45691, AI002022, AA430177, AF361746.1, AB060855.1, AF277292.1.
HHFHJ59	246	411332	1 - 647	15 - 661		AA833770, AW877426, AA804902.
HHFHR32	247	411470	1 - 1364	15 - 1378		AL537554, AI949994, AI417813, BE176604, AL337293, W63587, AA555104, AV735759, BF433756, AW473655, W55970, AW779675, BE245761, AI436026, AI697597, BF446687, BE222143, AA310582, BE244564, AA725099, AA451851, AA860527, W49508, AI096339, BE218117, AA232777, AI082094, AL538385, AI160565, AA805441, W49509, AV741987, AI095778, AL538384, AA465271, AI685283, BE328263, AA233859, N62880, BF477950, BF240776, AV740618, W67453, W26654, R66448, AA347415, BE879790, AI301421, AA910440, AA815180, AA947419, AW388859, BE176537, AA806906, BF796176, AV716929, H04548, AA743984, AW294389, AW978207, D80074, AA953439, H53694, BF935876, D82288, BF971117, N26986, AA057527, R14689, BF794295, BF213700, W55969, BE893895, BF931384, AV743289, AW612155, H04469, N77787, R42413, N40108, BF243047, AA988864, BF240864, BE836282, BF239091, BE243458, N79387, D80452, AA910721, AV654871, BE887608, AV753942, M85866, BF243539, AI016440, AV754341, AV753874, AA013030, R13766,

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HHFOJ29	248	112749 I	1 - 1352	15 - 1366	AA776789, AI190772, AA428791, AI025500, AI219913, AW082984, BE241726, AI219933, AA628326, AW204939, AI698565, AI809744, R28215, AA913953, BE242686, AA477200, AW505434, TI2580, AL157938.22, AK024434. 1.
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HHGQ54	251	544615	1 - 861	15 - 875	AL528163, BG252074, BF529806, BF855582, AA234290, AW264333, AL122942, AW293770, AA458524, R41805, AW338445, AW264239, AL091253, AW316552, AA454605, AL459366, BE299516, BF856403, R42539, AL698643, AL082503, BF436761, AL673224, AL864282, BG222925, FI1117, AW293131, AL446586, AW029153, AA568555, AL123718, AL352145, AA234190, BG251585, AL459970, R41441.
HHGDF16	252	579890	1 - 876	15 - 890	AL365221, AL701000, AW954119, AW264473, BF344449, AL680921, AL492007, AW014989, AL860823, AL539819, AL473662, AW628976, AW276150, C75362, AU152947, AA167428, AL559629, AL811077, AL039475, AL656542, AL284462, AW590370, AL431949, AL656530, AW148492, N67246, AL915180, AA907555, AA047467, AA478729, AL365222, AL242862, BE018520, AA834839, AA412178, BE302119, AL823337, BF671770, T61838, AW007865, AA905198, H08613, AL382420, AA776507, AA385375, T94765, T94766, AA047401, N53320, AW890140, BF949155, N83376, BE883645, AV701945, AV704429, AW890022, AW898540, AV702726, AV703584, AV703624, C01033, AV702464, AW890015, AW956618, AV655824, AV708871, AV729091, AV704729, AV656250, AV655597, AV701800, AV705652, AV703976, AV707059, AV705178, AV661490, AV727054, AV701616, AV709625, AW956781, AW964267, AV706912, AW890016, AV709236.

HHGDW43	253	554613	1 - 1036	15 - 1050	AV701584, AV726913, AV704346, AV728464, AV707827, AV693230, AV687808, AV705939, AV708600, AV705045, AV704029, AV702601, AV655568, AV727449, AV701067, AV727266, AV705517, AV650430, AV704588, AV702830, AV702086, AV728521, AV725260, AV951773, AV726646, AV703833, AV705813, AV729463, AV705474, AV703653, AV726903, AV725970, AV707500, AV728256, AL133418.4, AK023144.1, AF214114.2, AF208045.1, AF227899.1, AU122180, BE070260, BE070199, N47096, AA633840, N50530, N49396, W00508, AC079353.5, AL122002.16, AC004506.1, AK022355.1, AC004808.1, AC002112.1, AL355334.26, AL137003.12, AL157893.16, AC005084.1, AL136116.11, AC020613.33, AL160237.4, AL109954.15, AL589684.7, AC021699.5, AL022150.1, AL138773.4, Z83848.1, AL390035.10, AC008269.4, AC016770.10, AC007132.3, AL356213.10, AL132656.14, AL139332.8, AP000679.5, Z83820.1, AC016941.9, AL358975.8.
HHPD20	254	610321	1 - 1147	15 - 1161	
HHPGO40	255	129992 7	1 - 988	15 - 1002	BF936014, BF926087, BF849807, BG059559, AA663575, BE464797, AL137451.1.
HHPT165	256	490904	1 - 501	15 - 515	AL533025, BE464963, BF110244, AW085558, BF110283, BE348401, AI343272, BG149420, BE327679, AA719308, AW298394, AA425555, BF939779, BE669809, AI356804, AA719641, AA928881, AI458306, AA928875, BE221905, AI304915, BF064266, W52908, BF433114, R43953, AA235409, Z38804, AA890287, AI928712, F02482, BE503857, AW470411, BF940932, N63308, AW023387, BG149175, BG150134, H87740.
HHSDX28	257	553494	1 - 1099	15 - 1113	AA548981, BF835253, BF835251, AA854044, AI784057, AL034420.16, AC006060.1, AC025470.4.
HILCF66	258	636025	1 - 1654	15 - 1668	AW866442, N50805, AW769075, BF836507, AI206345, BF840986, AA708926, AA426062, AU155280, AW866532, AW769542, AI652458, AA258053, AA532374, AW674310, AI079267, BG178864, AI918893, AI833381, AI129768, AW151099, AI375855, AI077465, AI434984, AI084577, AA353483, AI803071, AI978803, AA435860, AA625163, BF437117, AI093544, AI016100, AI951676, AI684966, AI479709, AA502596, AA075493, AI224122, AA531263, AI865571, AA424807, AI337861, AI275719, AI784447, AI393782, AA045896, AI798537, AW627862, AI362624, AW188737, AI587550, AI583574, BE242408, AI951273, AA135691, AW514022, AI262711, BF939682, AA135723, H06916, AA398860, AI583554, N93804, AI707963, BF843408, BF843416, AL522362, AA625925, BF738648, AI919121, T98717, BF059218, AL526660, T98661, AW022094, D19802, AA887448, T25800, BF950460, AL529899, AA654911, W44832, AA426475, BF773449, AL529900, AA495877, AK023371.1, BC000630.1, BC000904.2, D14663.1, AF215935.1.
HJACG02	259	130778 9	1 - 561	15 - 575	AA311223, BF002026, N41594, N30820, BF982046, AI829327, BE047833, AI457369, AW071417, BF968205, AI340627, R36271, AL036980, BF061283, BG168549, AW022682, BG034550, AV682418, AL047042, BF343172, BG113299, AW020693, BF751308, AI452560, AI690748, AI349645, AW946806, AI340511, BF924882, AW074869, AW196299, AI038445, BE781369, AV302992, BG110684, BE887488, AL514193, AI310575, BG164558, AI340533, AI349957, AI343384, BF680133, AV715560, AI309401, AI345005, BG163618, AI343112, AV743962, AI826225, AI811785, AI494201, AI494201.

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HJBCU04	261	877643	1 - 1178	15 - 1192	BE559708, BE560064, BE561205, BE396781, BF975879, BE559864, BE267986, AW964091, AW084454, BF796667, AJ339413, BG106279, BF663626, AW964099, AA714519, BE267607, BE396583, BE267550, AA568144, AA312661, AW135205, AA767738, AA311112, AA252797, AA310964, AA977844, AA835549, AI832051, AA357111, AW971671, AA356801, AA746595, AI368885, AA380418, AA827647, AW407267, AW404968, AJ010059.1.
HJBCY35	262	719729	1 - 1545	15 - 1559	AL518865, AL526445, AL518864, BF690211, BE795952, BG261247, BG122941, BE871131, BF342499, BF797882, BG034854, BE874386, BF684303, AW958340, BF055513, BE265238, BF055496, AL042954, AL044311, AW393087, BF590235, BE251517, BF688851, AW500006, BF750912, BF436031, BE207255, AI523943, AI809559, AW615714, AI088845, AI199469, AI088821, BE792741, AA707004, AI393362, AI839578, AA864359, AI359119, AI963339, AA259086, AW027379, AA186786, AA703021, AA305929, AA393356, BE729570, AI961726, AW274049, AI216448, AW503180, AW505339, AI015694, AA291342, AI049539, AW873566, AI092749, BE410341, AI817912, AI870620, H44330, AI366215, AA258242, R46300, R16949, AI744596, R54656, BE386449, BE410337, AI807057, AW081887, AL041401, H15972, BE710574, BE410414, BE535502, BE222788, AA398688, AW273864, AA404987, D59795, AA077661, BE047327, T10451, AI871075, D59810, AI368575, BF526818, AA962247, AA335735, AW000813, BF435172, AA188015, R75708, AA329264, BE713106, AI218840, AA329538, AA291343, AA826970, T35806, R10855, D59833, D59821, BE547124, D80231, AI080034, AA299767, BF203222, AI908002, AA973311, AW087244,

HJMB118	263	545492	1 - 1007	15 - 1021	BF920764, A1648592, D80329, BE537114, BF511965, D59677, W93021, A1919083, AA749327, R16895, R55419, AA354448, AA136776, R54853, R46205, D59561, A1969256, W51754, AW273865, R10856, A1452772, BF765954, R10335, BF858687, AA076725, BF955782, BF206768, BF310354, BF032473, C01203, BC004286.1, AL050110.1, AB037861.1, AL137358. 1.
HJMBM38	264	545752	1 - 1010	15 - 1024	A1928477, AA527494, A1871626, A1694451, A1613494, N21002, A1630897, A1609811, AA987612, A1373242, AA595033, AW271584, A1858763, BF111620, AW975076, AA281453, C06206, H85386, C05666, AL536332, T23579, R22308, A125182, AA488619, A1914281, R45226, R37773, Z40129, AA658001, N66912, N78467, BE778573, AA211234, AL119049, AA928812, AC007622. 28.
HJMBT65	265	596795	1 - 607	15 - 621	AL518937, AL518938, BE410807, BE298018, BF663486, BF664523, BE741022, A1471526, A1624274, AW006720, AW072426, AA548389, A1805053, AA649964, BE295825, AW013989, A1889549, AL525865, A1380679, A1142829, BE796333, A1968598, AW006482, A1937663, BF475729, BE645645, BE958622, BF872663, BC002598.1, BC005015.1, AK022244. 1.
HJMBW30	266	491209	1 - 870	15 - 884	AW952560, BG168943, BE467261, BE177934, AW069580, A1890128, AW273443, A1744746, A1379922, A1522079, A1032260, A1279840, AA281064, A1879924, T66144, A171614, AW194179, A1085109, R55392, AA335275, BE178118, N99235, F09767, AA257163, AW972958, BF769935, AW293807, C02264, AA988919, AA357316, A1699614, BE936621, R47297, BF037710, AW881403.
HJPAD75	267	651337	1 - 1217	15 - 1231	BF689071, BE747537, A1922821, AW170567, BE906428, AA494514, BE879640, A1815043, BE673226, A1420757, A1751544, A1587576, BE223099, H28718, AA939115, W57617, A1143025, AA291927, AA291926, AW183956, A1587557, F26397, F29408, A1127566, A1565236, AA661632, BF765308, BF338229, BG034851, AW883883, BE774322, BF808197, AA211229, AC013356. 8.
HJPCP42	268	104029 7	1 - 1209	15 - 1223	AL530365, AL524811, BG035149, AL524846, AV653215, AL525028, BF031163, BE464161, BF064198, BG057645, BE677690, AV714679, A1954819, AA708718, AA773040, AW206827, BE677490, AW590005, AL522800, A1075390, BG179367, A1933314, AA022693, AA563665, A1582700, BF591973, A1933036, AA011394, BE463890, A1304827, AW467513, A1675049, N47573, BE537595, A1075392, A1346305, AL514603, W26975, H02832, A1290715, AA535130, AW137781, AW298065, BF927479, AA917670, AA011431, AL530366, AA974770, AA535120, A1497684, A1277012, A1274193, AL514604, AW297638, AW779938, AA356778, AW067366, AL524812, AL524847, BF763877, AV652546, H03723, F09604, F09318, H83110, AA216050, AW573003, BF926201, A1572540, AL525029, BF092250, D80466, A1940747, AK027129.1, BC008984.1, AF043945.2, AL163284. 2.
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HKAAE44	269	564406	1 - 1480	15 - 1494	<p>AL520657, AL520658, AL522597, AV681522, BE548729, BE899593, BE790785, BE792835, BE732295, AA034095, BF207081, BG104235, BG248527, AA099014, BE797840, BF149380, BF529516, AA443460, AA521261, BF128722, BE262937, BF149417, BE560958, BG231704, AI380466, AV708717, AL522596, AI601258, BE279990, BF972266, AI922591, AI568423, AA521360, AI340192, AA576296, AI018766, AI292077, AI149390, BE222604, N26097, BF683179, N56989, AA156490, AI751520, AI362844, AI092927, AI885624, BE409895, AI554676, AA443342, AI144510, AI361418, N39813, AW073509, AI300469, AI302840, AA054959, AA134109, N26662, AA836018, BE346367, AI660772, AA045420, AI763377, BE559554, AA999788, AW262496, AI148818, AA576417, AA961788, AI918062, AA045314, AA156140, H23879, N36737, AA887768, W01353, AA420615, AA102403, AA099091, AA055421, R40598, AI686531, BF222554, AI421021, AA363039, H47023, H42173, AA811052, AA631072, H85513, AI130256, AI969959, AI093973, AA702964, N62818, AI826514, AA443329, AI632688, AA357703, AI470639, AI918816, AI472869, AA829362, AI868052, AA809432, AI186580, AA568573, AI241611, H23880, AI216887, H46484, BE265435,</p>

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HKAAH36	270	135233	1 - 1202	15 - 1216	BE899189, BE747860, BE898407, BE898385, BE745465, BE388198, W73168, BE742856, AI002163, AW820357, W73140, BF513278, BE393948, AA862032, BE742548, BE272355, BF035167, BE746400, AW380655, N80762, BF033594, AW105502, W68496, AA292366, W68361, BF514439, BF350313, BE075958, AA394040, H43923, BC008036.1, AF168768.1, AF243527.1, AF135028.1.
HKAAK02	271	589945	1 - 845	15 - 859	AA552324, AA367607, AW827115, AL042753, AW772536, AV733824, BG122481, AI610645, AL042382, BF339483, BF792469, BE965355, BE965758, BF970990, AI686552, BG120816, AL042544, AA640779, BF339333, BG110517, AW967257, AI567351, AW089572, AW169653, BF885675, BF828567, BF339322, AV758110, BG257535, AV698087, BE965432, AV760391, AI696626, AV751784, AI4446373, AI872914, BE781369, AA613907, BG164558, AI801325, AL042538, AW074993, AI349614, AV652027, AI312152, BE544111, AI612759, BG112879, AI345735,

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HKAFK41	280	545018	1 - 535	15 - 549		
HKAFK66	281	946512	1 - 987	15 - 1001		

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HKMLM11	287	514788	1 - 940	15 - 954	<p> AU151371, AU159367, AU145655, AU154404, AU150750, AU152612, AU159804, W72741, AU146474, AU150684, AU152823, BE302039, AU152431, BE302186, AU1264916, AU152695, AU149949, AA599587, AW026884, AA626907, AA126630, AA581871, N70055, W94487, AA113220, AA938624, AI560420, AI870622, AU149957, AA226953, H97353, AU151073, AI097670, AI566990, F09549, AA610724, AA563737, AA974862, AW190045, AA669938, AU155526, AU150091, AU155518, AU155060, AA630115, AU150471, AW961280, AI191360, AI571896, R80426, AU154361, AI623459, AU156338, BE514913, AU150067, AA668477, N21455, R51577, AW969431, W31704, AI113390, BE673402, F04314, AW169427, AU156568, BG027127, T03630, AA858419, AU128655, BE889857, H17933, T40459, AA514726, F02328, AI491845, AI146488, AI864856, AU149654, BE244486, AI051351, AI922910, BF217017, T96369, BF196594, T65431, AI219701, BF541494, AU152028, AA599003, AA622745, AW593587, AW023946, BG032796, AI597830, AA214185, BF207819, AA088916, R49684, R74249, AA658944, BF576972, AI351009, AI132890, AA206322, AW149981, AA902464, AA205834, AI611206, R44358, AI865177, AI247836, BG115623, AA738215, AA888726, H05448, BF819090, AU149806, AW438971, R94411, AW875840, AW608777, AA668385, AA886478, AI969952, W95370, R45623, AA338507, R45342, BE871218, AI168677, AV655304, AA488788, AW369266, T80840, F35835, N90010, AI526392, AA776246, AA343900, AI934205, AA343877, W51983, AA319087, M77907, AW369292, H05148, AA527922, R72530, AV684723, AV685840, N83245, AA657347, AW747894, F27067, R06192, BF736297, AA824348, AW166672, AC008123.9, AK026166.1, M30938.1, X57500.1, J04977.1, BG036576, AW376266, AW024675, AW963560, AA946948, BE834077, AA306783, AV738527, AV739697, BF241514, AV740463, AA758808, AA431001, AA910368, AA336054, AA335971, AW237846, AW827285, AI050666, AV755459, AI583054, AA764946, AA459982, AI811603, AI683160, AV734888, AV721366, AA648361, BE397723, BF970114, AI336575, BF306639, F37462, AI872164, AV694812, AW301344, AA830333, AI633321, AA678887, BE876047, AV706721, AA563942, AI245332, AA653346, BE740632, AI360195, BG177101, BG026443, AA437293, AV698290, AV706279, AI933756, AW102858, AW022121, AV656973, AW582932, AW238753, BG110384, AI345143, AI224463, AA836317, AI047398, AI041154, AI814841, AI621106, AI436429, AI364620, BE620084, AI343119, BG109221, AA100151, BF796402, AV760181, AI349012, AI627692, AA765010, BE885490, AW021373, BG033906, AV756956, AV764180, BE011885, AI559654, AC005551.1, AF217998.1, U91329.1, AK026600.1, AF197929.1, AI137555.1, AI133093.1, BC007797.1, AC004227.1, U68233.1, AK027114.1, AI359583.1, BC007534.1, AI137662.1, X86693.1, BC002688.1, BC004145.1, AF217991.1, AK025549.1, BC005094.1, BC008196.1, BC006147.1, BC007280.1, AI512746.1, AK000632.1, BC000007.1, AF111112.1, X53587.1, AI136816.1, BC006481.1, BC001128.1, AV700405, AI433307, AI478641, BF115123, AI566076, AI522321, AW272244, BE048940, AW771517, AV686299, AA931216, AI522047, BE048682, AW302179, BF593517, AI493025, BE465247, AI733508, AI253208, AW269237, AI493090, AA994816, AW194908, AI470525, </p>
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HKMMD13	289	604751	1 - 929	15 - 943	AL389925.10, AC005386.1, AC010279.4, AL132641.3, AC008755.6, AE000658.1, AC009491.3, AL096772.5, AP000313.1, AC010148.13, AC008162.3, Z96074.4, AC007221.2, AL135961.4, AC009396.5, AL117338.15, AL137022.8, AL133173.19, AL121902.13, AC000194.1, AP001686.1, AP003113.1, AC006042.2, AL049715.25, AP001705.1, AC006606.5, AC002425.22, AL354864.16, AL445384.3, AC069262.24, AC017005.6, AC008178.3, AP002004.4, AP000684.4, AC008663.6, AL121977.11.
HKMMD01	290	527402	1 - 873	15 - 887	R69692, A1254831, BE439823, AW473380, AW967329, A1582769, A1076062, AA079635, AU148170, U95737.1, AC0072061.8, AC009032.7, Z84486.1, AF003529.1, AC008687.4. BE049073, A1252114, A1792903, BE063133, A1734002, A1307426, AW301818, BE049088, AV740060, AV738722, AW105737, AW851028, A1200051, BE049095, AW406755, AW361583, A1054246, AV756693, AV758600, A1792864, A1733957, AA610491, A1334443, A1053816, A1252085, AL138242, A1358229, BF668217, A4501784, A1954260, AW966759, BE147093, AW303196, AW301350, A1254798, AW419262, BG014866, BF308728, A1431303, BG249643, F29989, BG010083, AV703137, AV701499, AV706025, AV759204, AW086257, BE147117, AV763540, BE139371, BF970654, AW950632, BF725504, A1246796, A1016000, AW074398, AW474160, A1216978, BF873504, A1349874, AA663306, AU122216, AW969988, AW905746, AV682003, BF761328, AV761745, AW833862, AV733328, BG167743, A1754689, A1654529, BF436771, AW500125, A1801205, AW970564, A1890348, AW962713, A1623720, AA441788, BF773305, AW069450, AW276984, A1963720, BE042649, BF808370, AV729809, AL138265, BE049139, AW021917, AV728425, AL040072, BF676536, BF681427, AV704740, AV701613, AW271904, AV701844, BG167139, AA557879, F36373, AV760466, AV710606, AW023389, A1281807, AF074677, BF337291, AW472872, A1569202, BF827410, AV761810, BF887156, BF917533, AV762645, A1365988, BE540527, AV705518, AU147488, AW963497, BE139267, BE205860, AV710482, AL046409, T06828, AL048616, A1754013, BE349302, AV703266, BG231767, AW339687, AV725423, AA394271, AU146189, AU145473, A1754955, BF908593, A1345695, AL118911, AW028429, A1635272, BG033926, A1285615, BE909262, BE744242, BE293802, AV729000, BF058000, BE304890, AL041690, BE293845, BF769461, A1753365, AV725974, F32705, F36273, AA555260, AV762395, A1281808, A1355206, AA128592, AW236342, AV763971, AA366035, AA501614, BG010931, BG152682, AW503666, AA932099, AA744001, AW576389, AA581903, AW970848, A1282336, A1151261, BF869171, AV740801, BF241967, A1370475, BG176793, AV763583, AA515435, BF916567, AW839174, AW979060, AV764329, AW064321, AC010727.6, AJ300188.1, AP000320.1, AL513128.11, AC002429.1, AL162374.8, AP000120.1, AP000167.1, AP000052.1, AC009502.4, AP000099.1, AP000036.1, AC010719.4, AC012306.11, AC009247.12, AC010601.5, AP001719.1, AC000360.35, AC006288.1, AC004460.1, AC002369.1, AC021016.4, AL445683.11, AC005221.1, AP001718.1, AP001479.1, AC024164.6, Z86061.1, AC004873.3, AF045555.1, AC004087.1, Z93022.1, AC087589.2, M37551.1, AL160411.25, AL359986.15, D83989.1, AC020658.6, AL390023.8, AP000314.1, AL450320.4, AB020870.1, AC017033.5, AC083866.2, AC004797.1, AC020751.5,

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HL2AC08	291	610018	1 - 1464	15 - 1478	AL514822, AV716855, BE797339, BE889786, AW993482, BE778704, BE784148, A1064951, AW993281, AV649573, AW993282, BF030967, BG171338, BG253627, AW992854, BF339378, AV716022, BF699835, BF036931, AA670112, BF672645, BF214975, BF208494, BE567595, AA356542, BE003103, BG250954, AA356578, AA913737, AF090918, BG114769, AA353906, AA263131, AV736179, AW674899, AA732423, BE907740, AA356577, R79616, BF696689, BE080437, R34190, T72824, AA206943, BF209735, AA318503, BF700002, N78351, BF034898, BF340141, BF799849, BF210023, BE874285, AA471271, BE706224, BF034728, BE003256, AL080080.1, AB048246.1, AL591807.1, AC011290.3.

HL2AG57	292	695733	1 - 1766	15 - 1780	BE541697, AW955830, A1829139, AW264273, AW070588, AA872984, H06954, A1369038, AW134647, AA974445, AA902284, A1904699, H14753, BF110637, AW006498, AA970510, H06955, AW843696, AW885852, BF895113, AW243991, BF752088, AA306732, AW603435, AA333155.
HLCND09	293	117204 6	1 - 1970	15 - 1984	AL524488, AL516965, BF341800, AU118258, A1832149, BF341727, BE910678, AU152725, AA253498, AA927669, AW136320, BF966942, AA284897, A1341987, A1375638, A1141878, AA410733, AA724418, A1656580, AA626359, AA633990, AA210941, AA480438, A1499844, A1498056, AW135997, AA595691, AA209463, A1804771, A1189792, A1151483, A1242359, A1278938, AA456100, BG056746, AA602519, AA253394, BF347961, A1189792, A1151483, A1242359, A1278938, AA456100, A1831279, BG036545, N51328, AA455603, BF841465, H22614, BG056059, R55869, AA496421, W96552, AA284720, T16865, BF341594, A1913942, AA904546, R55788, R90922, R87952, R87953, R25653, AW594694, T16864, AL524469, H20796, A1673432, BE262953, BF313400, AU130842, BE383565, A1954640, BE314810, BE262857, BE909511, BF929734, BE383513, BG036698, BE274853, A1631375, BE262592, A1380914, BF312256, BE262689, BF313886, BF530315, BE262731, BF315588, BF316121, BE277386, AW896204, AA969376, A1123164, T06607, BE262961, BG056600, R90921, A1355743, R27502, BF953012, AA338810, BE388421, R90911, BF954780, AW975618, AV718692, AV718489, AV742732, BG170993, AV724520, D51799, AW966053, AV699550, AW978634, C14429, AW966531, D80227, AV718800, AW966062, AV699927, AV722801, AV720731, D80038, D80269, D80166, D59859, AW973307, D58283, AV719822, D51423, D59619, D80210, D80240, D80253, AV719324, AV720211, AV719557, AV699447, D80212, AW959570, AV723927, D81030, AW949656, AW949642, D80195, D80188, AV719468, AW975621, D80219, AV720203, AV719188, AW949629, AW966534, D80391, AW960553, AW959628, AV719783, AV720028, AW965177, AW949646, AV718844, AV720464, AV718770, D59889, D59927, D80196, AW966054, AV718440, C14331, D80043, AW949645, AW949631, AW949643, AW949657, D80193, D80366, AV742048, AV721386, AW965158, AV741220, AW949641, AW949633, AW949632, AV720791, AW973447, AW959582, D80024, AW949653, D80022, AV700889, AV720812, AW959202, AW966013, D80378, D59275, AW966041, C75259, AV723097, AW978661, AW949658, AW959597, AW949618, AV742735, AV742001, AV701335, AW975605, AV701043, AV701332, AV701017, AV701248, AW966050, AV701431, D80045, D50979, AV738340, T03269, AW949634, AW949655, AW973541, D50995, AW966043, AV718633, AV720654, C14014, D57483, AW964468, D59610, AV645389, AV742667, AV645344, AV701125, AV718931, AV701166, AW960465, AW964488, AW964737, AW966022, AV700229, AV719628, AV699669, AV701443, AW959799, D59502, AV719049, AV699746, AV681510, D80241, AV681491, AV720220, BC009378.1, AL353953.1, AK023117.1, AF271371.1, X67155.2, D34614.1, D88547.1, Z82022.1, AF058696.1, AB028859.1, U79457.1, AB002449.1, AF188698.1, BC004265.1, BC003104.1, AK025084.1, AB048954.1, BC002386.1, BC006198.1, AL389935.1, AL117432.1, BC007852.1, BC003614.1, BC007241.1, AL117416.1, AK025209.1, AF061795.1, AF151685.1, AL137480.1, BC003052.1, AY034001.1, AL122123.1, AB050431.1, AL110225.1, AB050510.1, AL133049.1, BC001098.1, BC004196.1,

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HLDBE54	294	836041	1 - 1208	15 - 1222	AF250847.1, AL450382.6.
HLDBX13	295	815665	1 - 1801	15 - 1815	AI632044, BF871813, BF747135, AW630757, BF873312, BF770534, BF813448, AI608881, AA101562, BE792267, AI687737, BF71639, AA513370, C75490, BF848642, AW999404, AA861308, AA890390, AA486100, AW190875, C75621, AW339937, BE871109, AW338261, AI799264, AI193265, AA149993, AI469580, AW936241, AI925871, AI002582, AI955238, AI333843, AA486163, AI241578, AA702259, T86963, AI263270, BE350662, AI093487, H57108, BE934125, BF747862, BF807059, BF813934, R01692, AA837819, BF849699, BE927881, AW936086, AA714224, BF984148,

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HLDNA86	296	135219 7	1 - 1332	15 - 1346	BF982559, BG034488, BE313144, BE794497, BE910635, BF314688, BG120997, BF969005, BF340441, BF306972, BE525733, BE875593, BF792430, BG030710, BE262728, BF315735.

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HLDON23	297	636083	1 - 1248	15 - 1262	<p>AL529086, BE904120, BF337766, BF345489, AV706125, AI681123, BF002270, BF055322, BE856092, BE305227, BE219427, BF438375, BG149525, BF057786, BF590112, BF196165, AI741848, AI636347, AI973055, AI554720, AI871117, BE220195, AI745311, AW192924, AW340966, AA706712, AI091179, BF445900, BE645773, AI677802, AI889659, AI804323, AI688189, AW673266, AI298377, BE046787, AA535027, AW612722, AI830304, AW675294, AI139157, AW089901, AA410579, AW073842, AW316637, AA417232, AA416567, AI827376, AI372513, AA411560, AW001905, AI796719, AW673062, AI334363, AI085075, AI400032, AI452964, AA308319, AI888902, AI400560, T33187, AA877699, AI332395, AI372512, AA485507, AA017127, BG178589, R85136, AV705959, AL526358, BG056798, H94860, BF476221, AW016699, BF594282, R18537, AA988884, AI925753, AA993373, AW953175, W05059, AI263531, AA282629, F29641, R01402, AA625328, AA126985, AA354334, H58095, BE251679, AW662030, AI559961, AW337874, AA282410, AI014243, AI671403, R41526, AA485352, R43109, Z39066, BF925559, F04091, R01401, W04796,</p>

HLDOW79	298	847396	1 - 975	15 - 989	<p> AV751453, BE871534, AA128150, AW375092, BF237662, BE155754, T25085, F17839, AW371533, N74669, AW058382, AW371557, BF063353, AL360256.1, AL117482. 1. AA702685, AA470133, AI640188, AA442232, AA442756, AI566333, AI452429, AA442897, AW015092, BE222033, AA868769, AW300514, R01436, AA429745, AA705797, R00763, AA398423, H79642, BF087494, BG259284, AA252129, AI298508, AW272706, AA316913, AA705374, AW860285, BF913689, BE885241, AA641818, AA805708, N49165, AA665587, AL040011, AV682124, AI538564, BE047833, AW673679, BG028116, AI537643, AI564716, AI927233, AI954422, AA653252, AI494201, AA808175, AA746607, AL118781, AA693331, AL514093, AI570807, BF725644, AI633125, BF871314, AI582966, AW152182, AI537677, N71199, BE886291, AW079432, BF970652, AI096771, AW021091, AI829495, AV758806, BE974031, AA504514, BF836158, AI244105, AV656903, AI521799, AI884318, AW089275, BG107566, BF039003, BF812961, AI623662, AA928539, AW051088, BE048235, AW162118, AW020419, BE875959, AW160363, BF965053, AW088691, AI915291, AA888196, BG026969, BG105501, AI500061, AV682403, AI500588, BE047852, AL120853, AI623941, AI621341, AL041996, AI890214, AI254727, AW162194, AW022636, BF751288, AI365256, AI567128, BE876011, BG115134, AI886055, AW059568, AI859991, AV743129, AI669864, AA830596, AW088560, AI473536, BE790023, AI871703, AW167021, AI539260, BE906584, AI589428, AW327693, AA502794, AV757293, AI554516, AI433611, AL043070, AI345688, AI432030, AI150993, AI918408, BF525834, AI434731, AL046926, BG107834, AI698391, AI932794, AL036548, AI859240, AI702073, AI538850, AI699056, BG029086, AI473451, AI619820, BF997967, AI370623, AI889189, AI890907, AV682366, AI536685, AI824576, BG255493, AL514627, AI433157, AL513755, BF971001, AI274768, AW020095, BG113385, BF672397, AW080076, AL513901, AV746791, BF766529, BE786834, AV735890, BF055737, AV729336, BF814450, AW090071, BG113299, AA225339, F35882, AA732937, BF686473, AI540676, AI670009, BF814072, AW952456, BF038002, BF680133, AW880037, AI287862, BE881711, AI934259, AV703169, AI815232, AI678688, AA832154, BE909009, AW168705, AI811422, AI335411, AI910639, AI582932, AI872423, BE963954, BG117375, AI249389, AV727787, AI915295, AW004595, AI579901, AW827289, AI591310, AI521560, AI610667, AL514721, BE966699, AI690687, AI587489, AV681579, AI539560, AA834534, AI866469, AV734185, AW968336, AL042954, AI334445, BG164371, AW025943, AW079409, AA568405, BG027679, AI538829, AW198090, BG251435, AI783997, AI242246, AI522052, AI923989, AL048644, AW238688, AW083374, AI933992, BG252914, AI950877, BE966278, BF811804, AI440239, BF724894, AI887163, AI868204, AI738854, W74529, BE138941, AI471429, AI345417, AL513743, AI628331, BC002444.1, AF195092.1, AB049892.1, BC004181.1, AL136844.1, BC000714.1, Z82022.1, AK000418.1, AF132730.1, BC007680.1, AK024538.1, AL122100.1, S78214.1, AK000421.1, AL353956.1, BC003410.1, BC003052.1, BC002413.1, AL117394.1, AL137627.1, AL162085.1, AK024546.1, BC001967.1, BC004310.1, BC003122.1, BC009294.1, AK026389.1, AL136766.1, AF218034.1, AK025092.1, AL117460.1, AF227198.1, AL133559.1, AL137267.1, AL049283.1, BC001328.1, AF114784.1, </p>
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HLDQC46	299	847397	1 - 618	15 - 632	

HLDQR62	300	753742	1 - 2558	15 - 2572	BE876197, AU133975, AW170131, AV723948, BG178057, AV652458, AW836234, AW608052, AA047046, BF104746, AA486037, BE395776, AW385580, AA488655, BE699041, AA932253, BG104619, BF671350, AA854943, AA418105, AA829456, AA243385, BE699051, BE936060, AI346694, AA418007, AA503398, AA053835, AW067836, AA878478, AI309218, BF820483, AA287990, W37960, AI401102, AI279485, W37900, AI423510, AA610711, AI050735, BF939011, BE699047, AA701403, W30974, AA017371, AW385388, AA911160, BF928600, HI0281, W32542, AA133579, AV721259, H81907, BE908122, HI1712, AA657490, H09562, R97956, BF810354, N68428, BF841567, AA018681, BF810349, AW838671, AW274397, BE699044, BF737894, HI7436, AA133578, T03483, BF529092, BE699011, R93915, T84200, HI0225, R97955, N91220, F09018, BE244933, BE697384, AW474873, Z43397, AA677745, F11358, AW838680, Z42508, H08994, HI1779, R18755, AW067888, H86384, R20010, R44826, T78746, BE546845, BF768165, AA676360, Z41104, R12303, R61069, H80952, H01770, BF362799, AA857228, BE092626, AW361033, BE246721, R12953, F11514, AA298600, AA233314, H82000, Z45386, AA047038, AA988879, AA776420, R61792, BF925722, F02025, H37922, AA946813, AA058662, BE793798, AA298811, AW954042, AI024907, AA515707, AA579408, C02381, H38137, H80857, AA190438, AA059270, AW953912, W32541, AI253018, BF755527, AA252608, H39230, BF087406, BF841077, BE699066, F09175, AW608049, R36072, AW607934, AW242636, F02790, AA018740, BE092426, N47523, AW951415, BE872758, AA670010, BF793691, H86054, BE699208, AA017201, AA059226, BE857637, BG011131, AA233315, AW169463, BE935974, AA910836, BF756516, AA504287, AA489248, AW452612, BE858890, BE699076, AA953019, AA191764, BF930488, BE746764, AA552521, BF932022, BE080981, AW385586, BE092405, BE047109, AW838675, BE074538, AB046801, AC026749, AC026437, AC010491, AK001799, AF274753, I.
HLDQU79	301	740755	1 - 1474	15 - 1488	BG256275, BE867624, BE907396, BE855521, BF034422, BF530803, AW959247, BE782005, AI126689, AI121446, AA757065, AW630129, BF768037, BE746763, AA206154, AA460401, AI276320, BF998689, AA295243, BE242732, BG035901, AL040350, BE242810, T86168, BF983867, W05088, AA347337, BG252443, AI133502, AF064093, I.
HLDQM43	302	846330	1 - 595	15 - 609	AA502331, AW444616, AA568450, AW592433, AA503839, AI017393, AW957011, T85589, T78178, T72043, T85588, AI699382, BF593574, AA299977, T86494, AW956056, AW605240, AA335186, AA551860.
HLD RP33	303	647430	1 - 598	15 - 612	AF000301, AF000045, I, AP000114, I, AC005080, AC004878, I, AP001717, I.
HLHFP03	304	460467	1 - 599	15 - 613	H46196, AI421986, HI9572, H46195, BF947135, HI9490, BF738481, BF994257, BF127477, AW139949, BF947011, AF321824, I.
HLHFR58	305	919888	1 - 1001	15 - 1015	R09539.
HLIBD68	306	778073	1 - 1008	15 - 1022	AL538046, BF975484, BG260893, BF062040, AW250850, AW954319, BG118275, AI633756, AI436560, BE646174, AA975057, AW302253, AI651397, AI825565, AI479926, AI635567, AI612806, AI640598, AI653427, AI248825, BF770160, AI333221, AA609320, AI916748, BF346659, AW001438, BF941021, AA397893, AI083783, AA399663, AA302889, AA484860, AI659648, BF222019.

HLICQ90	307	791828	1 - 1752	15 - 1766	AI692578, R49550, AW016187, AA393712, AI673346, D80738, D81106, D81495, D81643, CI5479, AI696498, CI5522, R42643, AI761655, AA302888, D81794, D81487, D60344, AA302884, AA302883, BF813253, AA091824, BE743563, N49704, AI476597, D81533, N87760, BE396027, AA352126, AA281538, AA280240, AL133447. 1.
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HLMBO76	308	626831	1 - 801	15 - 815	BE962422, AW027068, BE617458, AW978331, AW992560, AW274834, AW131841, N32595, AI917820, AI907429, AI610587, AI348386, R50855, T16683, AA807222, R42665, R45605, R15777, N47819, AI699177, Z39130, M85559, AB033057.1, AF275817. 1.
HLQBE09	309	520375	1 - 619	15 - 633	AI742329, BF109853, AA778549, AI764973, AC005225. 2.
HLQDR48	310	130772 6	1 - 975	15 - 989	AV655891, AV718605, AV690404, AV719284, AA923549, AI950351, AV656411, AV720179, AV654765, AV656119, AV697855, BF511595, AC011472.7, AF271350. 1.
HLTAU74	311	853614	1 - 1510	15 - 1524	BG003917, AI817406, BE545490, AW380189, AW161631, AW971418, AI732482, AI732481, AA506465, AA455434, AI791436, AA506457, AI791435, AA455961, AI805870, BG003913, BF889164, AW512931, AI791316, AI791270, BE892615, AA361022, T52193, BF091793, AA410873, AA376333, BE250549, BF149315, BE925340, AA410708, BE699783, AW890323, BE276496, N95142, AC008088.8, AC004702.1, AC006251.3, AC008569.6, AL132640.4, AC004707.1, Z98742.5, AP001717. 1.
HLTDV50	312	520231	1 - 756	15 - 770	AV712119, AV659712.
HLTEI25	313	396672	1 - 829	15 - 843	
HLTEJ06	314	543017	1 - 603	15 - 617	AL525142, AW274273, BE327124, AI885095, AI885299, AA085210, AW340136, AI985381, AI369742, AW086489, BE298417, AI476470, AI039658, AI034384, AI333584, BE298210, AA455921, AI287650, AW592624, AA456390, AI266556, AI672315, R14963, BF688522, AI310815, AW962407, AA902537, AW954994, AV707146, AW960308, AW952064, AW960237, AW965813, AW963378, AW963660, AV703158, AW955713, AV727916, AW955616, AW951707, AV705433, AW954006.

					AV708850, AW960276, AW959059, AV709232, AW958280, AW966031, AW957853, AW953868, AW952011, AV658299, AI525316, AV661286, AW959983, AW953763, AW955152, AV704798, AW958796, AV705319, AV707329, AW949779, AV690209, AV707196, AV726026, AW952328, AV725709, AW952583, AW951551, AW955710, AV703620, AW965530, AW959858, AV709786, AW967182, AW952579, AW963752, AV653846, AW959721, AV707171, AW964112, AW965730, AW962924, AW953575, AV709555, AW960299, AV727272, AW955088, AW967184, AW962934, AW958088, AW965839, AW960676, AV706655, AW954209, AW960579, AW954407, AW960587, AV656373, AW961228, AW956010, AV706407, AV702120, AW965759, AV652528, AW960201, AV727787, AV706925, AW951549, AV658784, AV726203, AW959366, AW955161, AV709025, AV708438, AW956762, AW949351, AV708007, AV726142, AW956138, AW951301, AV701657, AW954003, AV707422, AV729160, AW951750, AV727003, AV726619, AV705171, AV726755, AW963010, AW963641, AV727377, AW954427, AV728642, AV729557, AV702868, AV727526, AV725090, AV659389, AW954116, AW954238, AW950197, AV659294, AW960779, AW953499, AW958859, AV654287, AW951768, AV705665, AV705143, AV702574, AW954411, AV709587, AW959312, AW951184, AW957779, AW960049, AV702851, AW952192, AW963354, AV699089, AV660608, AV645504, AW954225, AW952329, AV655280, AV708320, AW954266, AI535639, AW951882, AV709314, AW950446, AV691080, AV687946, AV652001, AV728997, AV725745, AV684604, AW962980, AV728590, AV726737, AV704740, AV709660, AV701613, AW955707, AV701844, AW963643, AW958936, AV705538, AV706741, AW958529, U94592.1, Z30183.1, U45328.1, AB005666. 1.
HLTFA64	315	638242	1 - 1116	15 - 1130	AA703489, AW235215, W91995, AW361011, R99300, W91994, AA130677, H55848, T86395, AW051213, T86296, H5757, Z25051, AW579310, AC025754.4, AC016602. 6.
HLTHG37	316	787530	1 - 3726	15 - 3740	AL521709, AU139605, AU133158, AU139786, BE535428, AV715927, AV707854, BE882531, AI433464, BE302408, AW612477, BG122886, BE220521, BF593222, AI186034, AW189879, AA480343, BE002782, BF675617, AI082537, BE002805, AI745058, AI379721, AA001791, AW118778, AU149758, AA001870, AI190938, AA017469, AI810133, AI580107, BF061454, AA017470, N75111, AW573126, BG119005, AA496528, AI361074, AU143997, AI421480, AI797293, AU155671, AI039242, AA676895, AA035158, AA813771, AI380129, AA577557, AI625511, AU118630, AA034943, AA496455, AA035159, BE930108, H09058, R60578, D52456, AI199837, H71368, AA526250, H71321, H49158, AI801119, AW051381, AW193626, AI469299, Z44640, AU158178, AI375966, H03188, BE768068, AL537252, AW027677, BE769432, H03987, AA189113, F07896, AA884440, AI247826, BF112089, BE768175, R44612, AI370691, R41912, BF908980, AW338918, AA300907, AL521710, AI682819, F05975, BF911500, AA089462, AI755046, H08357, C00830, AW137909, H49079, BF594512, AI219213, AI902677, AW837163, BF335290, AA629557, D20866, T84855, H01516, AU127032, N92073, AA034942, AA384103, AA386034, BF758104, AW820302, AI758883, AI032167, AA136525, BF239017, BE073835, AL121716.16, AL117443.1, AK023709.1, AK023685.1, AK001365.1, AF180371.1, AF102265.1, AK023432.1, AB032081.1.

HLWAA17	317	629552	1 - 983	15 - 997	BC001258.1, AL162056.1, AL050080.1, AB029040.1, AK027030.1, AK021676.1, U52077.1, AL050341.18, AC003977.1, AC006249.1, AL080315.18, AC022425.6, AL162711.17, AC012172.6, AL139188.14, AF104257.1, AC004385.1, AF314060.1, Z84470.1, AF205406.3, AC025898.9, AL139385.12.
					AL522002, BF305304, AL521608, BE732838, BE899550, BF344719, BG115015, BG109203, BF982386, BE410162, BE735023, BE901175, BG117962, BE281306, BG165427, BF793440, BE901577, BE872442, BF316646, BE409982, BF982251, BF970528, BE262711, BE299415, BF340859, BE386152, BF569778, BE281612, BF305644, BG251248, BF673757, BF183244, BE547252, AL521166, BF237978, BG249255, BE280374, BE301893, BG109330, BG164142, AL522550, BE018945, BF170896, AW732476, BE018944, AL532064, AW250139, AA580387, H20615, BE741195, BE736037, BE272171, A752100, BE870251, BE742694, BE883834, Z42865, W21970, AA873793, AW579408, BF753347, AA204913, AA206511, AA158660, BF971112, H66924, R25678, AA233944, BE743048, BE743976, BF304498, BE546682, BG112068, BF317329, BE278514, BF878947, BE744899, Z25248, BG248593, AW675147, T56764, AA368717, BE793472, AW956985, BE246887, BE298316, BE410692, BE707861, BF125052, BE388318, BF970723, BF675911, BE868990, BF031826, AA380216, AJ271671.1, BC007886.1, BC002563.1, AJ243649.1, BC003152.1, AF151829.1, AF132942.1, AJ243650.1, AC004832.3, AC005585.1.
HLWAA88	318	588485	1 - 1756	15 - 1770	AI075040, AI566035, AI346970, AW453036, AU136077, AW572319, BE677521, AI971962, AI354722, AI611131, AI285086, AI017423, AW612105, AA719963, AI493120, AI910743, AI346087, AA860835, BG055741, AA995966, AW235992, AI188298, BF740313, AI205497, BG055743, AI949884, BF851530, AA939291, AA883259, AI985431, AA070019, AA613006, BE075994, AK023527.1.
HLWAD77	319	653513	1 - 1153	15 - 1167	BG250493, BE786038, BF968793, AI148564, AV714668, AI911259, AV717040, BF031366, BF970799, W60958, BE221213, AV701362, AI683823, AW268612, AV711084, AW275920, BE551456, BE551386, BF244446, BE550880, BG110482, BF669035, AA404358, AW956755, BE669452, BE504275, BE674209, AV763474, AA443743, BF381847, AI271616, AA936391, AI675766, AV703458, AI695003, AA403095, BF968311, AI311856, AI082141, BF036575, BF575757, BE905833, AA503819, N30670, BF027805, T86418, AI079408, AA393808, AV711478, BE872085, AA393892, AA827290, AI189388, AA910984, R21152, H96780, AW804422, AI014740, AA804216, AV714823, AI219049, H23300, AI566294, R99539, BF724670, N75557, R99538, AI299755, AA476793, AA974212, AA417638, AI374805, AW952564, AV725011, AI094470, AI133161, BF221760, W05584, AI089034, AA905867, T86508, AA677753, R99550, BF753822, AA335337, AI240536, AA313386, AI538267, AA918453, BF811514, H23186, H92649, W87796, AW445161, Z40615, BE272827, T33983, AW298229, R08382, BF475310, R08329, H97711, H96103, H80948, T99199, N24555, AA375092, T99198, H92437, BE260997, AA383378, BE536680, AI085108, BF920784, AF132289.1, AF242523.1, AK024574.1, AF151859.1, AC004148.1, AC024082.6, AC009263.6, AA419545.

HLWAE11	320	783071	1 - 1604	15 - 1618	AI344312, AI276017, AI476822, AI139478, AI160906, AI240398, AW001088, AA425919, AA011278, AA428788, AI354692, AI089176, AA622689, BF431807, AI968918, N68826, AI467807, BF436247, AW673768, AW135943, R24434, R16812, R31419, R24435, H83155, AI865939, R31418, AW673133, W67349, R31433, AA027080, R28030, BE542160, T81223, AI631986, AA677315, BF760063, AI872675, BF331923, BE926682, BE926741, AF329842.1, Z82188. 2.
HLWAO22	321	587270	1 - 1324	15 - 1338	AL515814, AL515776, AL534165, AL520605, BF342613, AI064806, BF528629, BE856301, AI140344, AI763061, BF063934, BF244655, BF683133, AW340290, BF344711, AI659614, AL515777, BF034915, AI554886, AI086027, BE929854, AW193974, AL515815, AI525649, AA410368, AI937139, AA918821, AI218197, BF313091, AL525747, AA829365, AI336469, AW473975, AA577435, AV645326, AW070946, H22929, AA722774, AI610462, T90764, AA404313, AI623603, R54057, AV723824, AA404713, AW168607, AA079100, AV752738, BF316436, AW402756, AA912779, BE742923, AL534166, AA609213, BE350786, AA406191, AA923714, AW750290, AA325220, AW952354, BE898647, BF092248, AA293154, AI218895, AI198020, AI672973, BG002684, AA649195, W81523, H08723, AW207732, AA927962, AI873660, AA774521, BF880685, AL520606, BF837510, AW794716, BE044401, BF767735, AI383372, AI204653, AI361791, Z39695, BE673415, H70703, R54056, AI187740, H24109, AA079003, AI867628, AA330197, BF310103, BF854730, BE797091, BE737142, BF541812, AI689520, AW297870, BF965605, AW590611, H08439, BE263819, BF086702, F02166, BE547512, BF115405, AA477404, F04433, T83213, BF036962, BF767508, BE795356, AA430434, AW797192, AA479566, R16340, BF678079, BF685049, BF847264, BF847254, BF804160, BF847373, BE904852, R41416, BE312226, Z45578, BF733974, AA971991, W81639, AI902460, BF833057, BF804096, AI903581, BE798202, AA433110, Z42682, BF917644, AI564885, AA335484, AI811209, AW083638, BE260879, BF314999, BE274089, AI903535, AW376204, AI755186, AI880283, BE540568, AI523835, BG165048, AI627893, AW008226, AI440284, AI568293, AI559296, AI954721, AI446511, AI934011, AI364167, AI538564, AI744268, AI688858, AV750565, AI539800, AW129264, AI540179, AI364589, AI638644, AI690784, AI499570, AI590043, BE966550, AA659690, AI829432, AI932739, AI719817, AI500061, AI873604, AI479292, AI244360, AI141406, AI633125, AI620864, AI866040, AI515021, AI885982, AW081383, AI824746, AI620056, AI269469, AI270448, AI274655, AI884318, AI287252, AI678446, AI651840, AI890183, AI701097, AI635634, AI763414, AI370623, AI476478, AI266652, AI696714, AI799968, AI628325, AW236186, AI653402, BF035033, BE963355, AW151714, AI637584, AW055081, AV703776, AI866893, AA836665, AW152182, AK000833.1, AF226048.1, BC000659.1, AJ289857.1, AL110160.1, AJ297977.1, AJ289848.1, AJ289856.1, AJ289847.1, AJ289849.1, AJ289846.1, AJ289851.1, AJ289852.1, AJ289854.1, AJ289853.1, AJ289850.1, AJ289855.1, AK026408.1, AL117587.1, L25851.2, AL136850.1, BC004349.1, AL050149.1, AF183393.1, AL133619.1, AL162083.1, BC008591.1, AJ299431.1, BC009360.1, BC001785.1, L19437.2, AL080159.1, BC001711.1, AK000027.1, AL512684.1, X99971.1, AL133084.1, AB055331.1, BC001336.1, AL389935.1, BC004373.1, AL389982.1, AL133062.1, AK027209.1, AF115392.1, AL049959.1, AB056420.1, AL137530.1,

HLWAY54	322	658702	1 - 1878	15 - 1892	AF122922.1, BC000732.1, BC005070.1, AK026462.1, AK000418.1, Y14314.1, AF124728.1, BC001199.1, AL050138.1, AF217973.1, AF131821.1, BC002849.1, BC006345.1, AK000484.1, BC008649.1, BC007641.1, AL157479.1, AK000414.1, AB060897.1, AL080154.1, AF353673.1, AK024974.1, BC007571.1, AK026182.1, BC005123.1, AK025658.1, BC001760.1, AL080148.1, AL133559.1, AB011076.1, BC007364.1, BC008063.1, AF267739.1, BC003101.1, AF218000.1, X99270.1, AL137682.1, AL138832.10, AP001601.1, AP001698.1, AB047878.1, AL137533.1, AF061795.1, AF151685.1, AL1359583.1, AL137254.1, AC004805.1.
HLWBH18	323	104519 4	1 - 799	15 - 813	AI024421, AA424694, AA824340, AA864327, AW592506, AA496077, AI125678, AI028208, AI126598, BF091360, AA406076, AA443593, BF376146, AA709069, AI131223, AI141116, AI333624, AI333870, AI769240, AI091519, AI147148, AI122673, AW948495, AA471063, H30251, R07741, AI138894, AA993247, BF376156, AA405433, H30315, AI382680, R07740, AA992230, AL042116, AB051833.1, AF085884.1.
HLWB163	324	566842	1 - 1024	15 - 1038	BG000096, AC023490.5, AC018636.4, AC006435.7, U95742.1, AL121891.22, AL451142.7, AL035659.22, AC020716.3, AL136179.15, AL450339.5, AC007216.2, AL136418.4, AL139054.1, AC011533.6, AC000159.6.
HLWBK05	325	765310	1 - 2369	15 - 2383	AI042019, BE858742, BE855466, BF476111, AI906495, AI908477, BE674293, AW274510, AI560883, AI989629, AW473428, AI680172, AI339026, AW612370, AI418979, AI275052, AA767349, AI890489, AW021884, AI969094, AW977119, H89111, N93142, AA885772, H10993, BE181184, AW368289, AI567013, AI868712, BF132001, Z40983, BE564470, H95610, R39509, BF695232, AW853314, W38986, H92044, AC008040.7.
					AL536493, AL514199, AL157671, BG260370, BE379053, BG252836, AL529147, AL515380, AL514200, BG104666, BG114729, AL529146, BF967759, BF527200, BF316407, BG261268, BF184232, BF115962, AW965314, AW005623, AW973905, BG171109, BE736594, BF529773, AI928466, AW516590, BF966979, BE046448, AW014546, BE876855, BG254307, AW958252, W87297, BF526617, AW959008, AA164613, BF439848, AW000936, AI703274, N24392, AI580919, AA037159, AI686912, AA179191, AW594515, AW085214, BE671804, AI168495, BE296633, AA868707, AA225014, AA888872, AI219983, AA179201, AI660755, AA164612, AI334991, AA420527, H97664, AW510978, AA988373, R70657, AA576605, AA437178, AA628293, H10567, N36611, BF966853, AA970653, AI806255, AA224953, BE296638, W39077, AW242291, AA594662, H99143, AW078769, AI679580, AI269095, N94194, AI680017, AA844022, H23755, BF966096, AA602349, BE164717, N99359, BE328493, W87353, R46707, AA889625, AA573514, R77834, BE090735, N25981, R51410, BF247470, R25551, AA398028, H80504, H48364, AA470783, AW207718, H06507, R64682, BE904435, AA426463, R12724, H06563, R64681, N63835, BF377563, R39776, R16671, BF966194, AA332170, AA378783, BF353343, AA609145, AA887867, H60238, H48275, AA360706, AI208801, BF884388, H11082, BF361356, AW238918, AI886136, R51298, R20363, N89819, H81420, N48366, AL527159, AV691174, BF361358, R40704, AW795836, AA704248, BF884528, T03502, C01112, BG055466, R41078, AA927831, AA988831, R75935,

					R31994, AA420594, R43748, AA356016, AA350100, AA639019, R16672, C14942, BF963256, AW947442, N71425, H60193, BE694187, BE694204, AA376032, BF358985, AI475079, R13270, AI872772, AW627454, BE841315, N55971, BF348486, AA938370, BE906485, N49143, BF370548, BE841319, AA169181, AA169309, BF204852, BE881724, AW051264, BE937060.
HLWBY76	326	797609	1 - 2067	15 - 2081	AA923172, AI139607, AI269739, AI802946, N30680, AI277957, AI277237, BE715040, BE838082, BF354274, AW797336, AW797335, BF987948, AW873630, AI806044, AK076806.1, AC003991.1, AK027807. 1.
HLWCF05	327	460619	1 - 632	15 - 646	AW673972, AA524980, AI961840, AW515257, AA877458, AI336752, AW070880, N66443, AA528268, AI273991, N26777, AA004802, BF990906, AA700372, AI290414, AA906772, AI243008, H17960, AA502507, AA860313, AW470183, H84037, BF348530, R54094, BF764578, H84462, R30859, BF764695, AI864306, AW022917, AW970612, D45536, AI908718, BF878700, AW999226, BC003414.1, AL450487.17, AK025020. 1.
HLYAC95	328	778075	1 - 298	15 - 312	AV764526.
HLYAF80	329	460622	1 - 812	15 - 826	AA972709, BG111199, AI499555, AI872315, AI924051, AI494201, BF812963, AI804505, AI815239, AI500659, BE883591, AI866465, BG167830, AI815232, AI801325, AI866691, AI500523, BF812438, AI538850, BE885490, AI887775, AI582932, AI284517, AI923989, AI872423, AI590043, AI500706, AI491776, AI445237, AI926593, AW151138, BF811804, AI289791, AI521560, AI889189, AI500662, AW151974, AI285417, AI623302, AW172723, AI539800, AI284509, AI582912, AI538885, AI440263, AI889168, AI927233, AW058275, AI866573, AI633493, AI434256, AI431323, AI866469, AI805769, AI434242, AI888661, AI500714, AI284513, AI888118, AI285439, AI436429, AI859991, AI889147, AI355779, AI623736, AW194509, AI581033, AI371228, AI798359, AI590024, AI491710, AI431307, AI440252, AI687588, AI440238, AL047422, AI567971, AI866786, AI860003, AI610557, AI431316, AI242736, AI828574, AI539260, AI887499, AW151979, AI539781, AI431238, AI537677, AI702065, AI539707, AI885949, AI285419, AI559957, AW089557, AI521571, AI469775, AI866581, AI567953, AI047398, AW074057, AI815150, AI446495, AI889191, AI952433, AI867068, AI225248, AI358271, AI698352, AI282249, AI371229, AI440260, AI474699, BE612681, AI687607, AI932620, AI890907, BF811802, AW129310, AL515185, AI866458, AI432644, BF815930, AI273179, AI499478, AI371251, AI866510, AL134524, BE897632, AI866461, AI923046, AW151132, AI049859, AI539771, AL048403, AI955221, AA878808, AL119511, AL513655, BF814072, AW151136, AL043152, AI273116, BG252929, AW858243, AI371237, AI561170, AI554821, BE895765, AI690946, AI469764, AI358612, BE877142, AW191003, AI648567, AI433157, AI433155, BF814447, AW081103, BE909406, AI538883, BG029667, AI801286, AL048375, AW021373, BF527274, AI867066, BG113493, BG260144, AI362495, BG110517, BG168696, AI371243, AI500683, AV736134, AA857847, BF892773, AV736402, BE963035, AI635331, AV743129, BE896091, BG257535, BF911528, BG033906, AL039390, BF795712, AI493559, BF796402, AI049850, AL045626, AW858522, AI274759, AI355008, BF036448, AI433976, BG254745, BE875243, BF726204, BE779152, BG169065, AA437293, AI049851, AI440236, AI282247, AI249936, AI963849, BE537531, AI539863, AI582910.

						AL040459, AL366900, AL537943, AL559976, BF814504, AW020095, AL366910, BG259737, AL521566, AA715307, AL513725, AL561177, AA809974, AW197139, BE618455, AL514283, AL250646, AL047611, BG113712, AL888022, AL512454.6, AL133391.5, AL138767.15, AL355795.13, AP001835.4, AL355136. 19.
HL YAN59	330	135220 3	1 - 756	15 - 770		AT761381, AT738617, AA777274, C02420.
HL YAP91	331	553514	1 - 1262	15 - 1276		AA464480, AT738416, AW970172, BF346852, BE004609, AL097351, AL051171, AW085704, N50904, AL950137, AT718945, H64092, BG236491, AL964070, AA514204, AW401489, W76242, H64144, AW204133, AA295625, AW388106, BF751672, AA693868.
HL YAZ61	332	135216 3	1 - 1223	15 - 1237		AV653286, AW591154, AV653266, AV757663, AF002986. 1.
HL YBD32	333	566657	1 - 1031	15 - 1045		AL290473, N36404, AL804254, AA321183, AA258620, AC073655. 26.
HL YES38	334	638042	1 - 1209	15 - 1223		AV701925, BE883545, BE250577, BE736918, BE616582, BF793477, AV706319, BF338817, BF346135, BE728115, BE615376, BG250960, BG032917, AU139668, BF951636, BF811794, BE899007, BE898175, BF217767, AL133895, AA225638, AU121535, BE531051, AU135520, AW899342, AA601152, BF675027, AA601227, BE154390, BF911201, BE385152, BF680445, BE264980, BE386373, AA715194, BF874267, BF871285, AA826146, AW023095, AW957880, AW957801, AW962273, AV732690, AA307661, BF882363, AW845664, AV749263, BF197329, AA779025, AA489803, AW872342, BF815608, AV748578, BF957961, AL380547, AA833581, AA243106, AW939910, BE304382, BF877837, BE141836, AV750972, AW962826, BF982391, AW938878, AU116940, BF203663, AA503299, AV652861, H02956, T47541, BF763870, AW865469, AV731015, BF207674, AL940701, BE184422, AA280232, BE792178, BF829537, BF767788, BF957954, AV683302, AV698434, AA258511, AL918674, AA121877, T07838, AA804919, AW515786, AA281292, AW865403, AU140348, BF238662, AA353112, BF732306, BF940980, T84195, AA431655, T06482, AL440300, H67786, AV715734, BE565499, AA630813, BF673583, AT761174, BF812273, AA593381, N62150, AA487808, W22010, AW898213, AW963317, AV653743, H67930, AL940708, AW864780, AA359714, AL052560, T07383, AW899527, AW999271, AW845678, AA649067, AW898920, AA356190, T97032, AA434462, AA221018, R01106, AA418919, AA431294, BF873657, AW630075, H73439, AA583363, T81895, T47477, BE177666, BE083070, BF951580, AW845665, AV729748, AA720812, AA577789, AA173218, BE968449, BF096068, BF869076, AW893125, H47099, AV730261, AW409222, AC005166.1, AL133514.7, AC005588.1, AL355143.17, AC004045.1, AL450333.13, AC008962.8, AC005768.17, AP002853.3, AC009466.17, AP000880.4, AL157688.4, AL121939.12, AC010369.6, AC004946.1, AL139327.18, AC011198.2, AL135780.11, AK022205.1, AC069304.7, AL109769.4, AL049781.5, AP001669.1, AL355520.8, AL133517.11, AC026398.4, AL353133.7, AL357153.4, AL049796.28, AF002997.2, AL356498.10, AL360020.15, AL121958.6, AP000826.4, AL590964.8, AL022399.2, AL121949.13, AC007065.5, AC023154.5, AL008722.16, Z82212.1, AL138965.10, AP001179.4, AL360272.23, AC006379.2, AC034215.4,

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HMADS41	335	596831	1 - 1253	15 - 1267	BE740695, BE739906, BE899124, BE742745, BF685920, BF971897, BF684948, BE336652, BE747520, BE925550, AI733012, AI492192, BE207602, AW275042, AA954656, AW139807, AI791409, AW136444, AI361524, BE207644, AI762361, AI762373, AI246377, BF684146, AA306161, BF062047, BF222947, AW003832, BG028044, AA865078, AA402599, N32269, BC007725.1, AF123757.1, AF123758.1, AF123759.1, AF123760.1, AF123761.1, BE736177, BF968408, AW953455, BE513085, BE889654, BG248447, BE910370, BE311470, BE905308, BG163998, BE744428, BG167712, BG167766, BF219830, BG181007, AI141537,
HMADU73	336	135217 7	1 - 3180	15 - 3194	

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HMDAM115	337	135240 6	1 - 1244	15 - 1258	BE790239, AI114496, BE047613, AI609021, AI478544, AI949665, R96283, AI205799, W39248, AI670908, T70976, AA070919, AI243978, AW854183, AI796472, BF883407, AW975683, AA654405, AI125888, AA730911, AA545731, BE222003, AA730927, C21177, AA721678, AI478489, AL137139.9, AL139035.27.
HMDAE65	338	520338	1 - 684	15 - 698	AL035447.6.
HMDAM24	339	514394	1 - 982	15 - 996	BF741516, BF740289, BF740290, BF741538, BF760315, BF911969, BF830586, BF759998, BE083615, BF932902, BF763222, BE079695, AC004797.1, AB023141.1.
HMDAQ29	340	600406	1 - 960	15 - 974	BF828645, AC007404.4, AP001064.1, AL158172.5, AL096700.14, AP001754.1, AC011446.6, AC021325.5, AC016968.24, AL008719.1, AL031729.16, AC008011.11, AC074295.7, AL157823.9.

HMEAI48	341	135229 0	1 - 399	15 - 413	AA297104, AA298556, AA216561, AW957476, AL532709, AU124631, AA173361, AA206770, R14826, AL513976, BF726195, BF901681, AA873180, W20303, AF109127.1, AF109126. 1.
HMECK83	342	636035	1 - 996	15 - 1010	AW070189, AA680237, AA577812, AT732177, AA835854, BG223537, AL023494.12, AL158196.24, AC009102.9, AE006466.1, AL163248.2, AC003957.1, AC008537.5, AC022161.7, AL357315. 14.
HMEET96	343	566720	1 - 1323	15 - 1337	AL521371, BF337502, BG249151, BG113640, BG260630, AL521372, AL516032, AV731587, BE384522, BE973743, AT735261, BE563906, BE277846, AI808277, BF667795, BF691333, AW958349, BE871082, BF791366, BE389571, AW674769, BF691310, BF743166, BF211360, AI368797, BF572289, AA583057, BF664548, BE567499, AA807741, AI828551, W02860, AI088857, N44490, AW439214, AI026716, N73457, AI142511, N34764, AA633495, BF346426, AA594963, BG258660, AA862351, AI356184, AW518053, H98681, AI125040, AI306645, AW675383, AI280832, AV729211, AA748024, AT707840, AA830528, AA916426, AI285008, BF743169, AV724056, BE531141, H04537, T71560, T87237, BE855394, H29267, T71330, AW078897, AA507967, BF790198, AA613581, AA215785, H09795, AL516031, BE763380, T71482, AI261966, AI783537, AW853901, T79791, AW853890, AA459511, T97835, D60812, AV711819, H04458, N27248, AA483615, BE615442, AI685127, BE616237, F10230, BF239991, BE614864, BF965165, AI471017, T79360, C00631, AI523786, BE833176, AI587003, AW051263, AA588437, AW364142, T10196, AA379077, H57434, AI469848, AA156281, R41344, BE077173, BF239125, H94779, BE093345, AW168908, BF541751, T74091, H09880, H29351, BE833069, T82010, AA082465, AW951663, AI919531, F12612, AA452714, AW068971, BE697991, AA450068, AW024907.
HMIAL37	344	603201	1 - 1406	15 - 1420	AW934844, AL045824, AI269960, AW300030, AA860926, AI761354, AI739238, AW351654, AI984995, AW390711, BF931410, BE464037, BF229829, BE764327, AI628985, AI989344, AW013904, AI869919, AA121174, AI453367, AI270726, AI272081, AI869907, W22160, AW192301, BE463416, AI991419, AI796741, AA551799, AI738967, AI738958, AI783811, AW304132, AA344913, BF229794, BF798430, AW843500, AW888833, BF798442, BE763828, BF761128, AI121198, BF333846, BF928080, AW062449, AA327309, BF800375, BF800393, AW845326, BF808207, BF819298, AB018687.1, AB006955.1, AF039700.1, AF039699.1, AC005137. 1.
HMIAP86	345	726831	1 - 1660	15 - 1674	AL533220, BF967956, AL533253, AL520510, BE735407, BF972030, BE735149, BE615619, BE616472, AI873527, BF347687, BE383692, BF967233, BE385645, AW593348, AW381588, BF541528, AI032869, BE294015, AA404241, AL564151, BE294088, AA401224, AI682367, BF694848, BE255192, AA910774, AI367739, AW976142, BE615232, BE389860, BF029472, BE615138, BE645680, AI131262, AA054608, AI479085, BE728074, BF672705, AI241428, AA021119, AA142931, BG108596, AI039086, BF348256, AV748480, AA021118, AA056945, N48177, AI202193, AI491859, N53324, AI364707, R44688, AA015735, AW015622, AA905989, AA813639, AA057005, AA035652, AA917010, AI952221, AA054548, AA015832, AA505774, AI697106, R19440, BE707409, BF841914, BE677828, AW954134, AW950006, AW954211, AI968179, AW960629, AW964070, AV728721, AV656478, AW953797, AV696931, AV683994, AV703878, AV702019, AV705014, AV728733, AV727510, AV706741, AV726026, AW952460, AV709596, AV709273, AV725633.

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HMKCG09	346	548078	1 - 907	15 - 921	BE043082, AI927692, AW058564, AW055230, AW015122, BF592005, BF196476, AA814450, AI634533, AI139038, BF446797, AI277016, BE045365, AA732327, AI435146, AA290626, AA832487, AW964897, AV682305, W56110, AI796930, AI949631, R48833, AI800208, AI628443, BF431339, BF371245, AI935532, AI582596, AA319436, AA832489, T59460, AA806730, AA279760, AA325502, AI935529, C20681, T59406, AA766259, BF089238, AL035209.1.
HMM/AH60	347	562776	1 - 808	15 - 822	AA736481, AI288032, AC004587.1, AC004031.1, AC002073.1, AC009137.6, AF001550.1, AL109628.5, AL121594.6, AL133215.16, AC024584.5, AC007688.15, AC005874.3, AF134471.1, AC002565.1, AC004678.1, AC003950.1, AC007546.5, AC002395.1, AC011529.3, AP002906.2, Z83826.12, AC009470.4, AC004703.1, AL050335.32, AL117354.12, AL136418.4, AL139054.1, AC005914.1, AL022313.1, AC002044.1, AC020633.3, AC018758.2, AC007279.4, AC013734.4, AC019205.4, AC005844.7, AL033519.42, AL035460.15, AC011484.4, AC020916.7, AF176815.1, AC007390.3, AC007371.16, AC009488.5, AL162615.13, AC006263.1, AC005156.1, U78027.1, AL031681.16, AC011491.5, AL136219.17, AC004383.1, AC002978.1, AC027319.5, AC018648.5, AC012476.8, AC055120.5, AL035422.12, AF031078.1, AL136218.26, AC008521.5, AC083871.2, AC074121.16, AL356915.19.
HMQDF12	348	566844	1 - 692	15 - 706	BE616124, BE616155, AW170508, BG009649, BF435220, AA573938, AW081928, AI961488,

HMSBX80	349	597448	1 - 1712	15 - 1726	AA159477, BE292792, AI674909, AW572265, AI923587, AA636061, AW089967, AI457146, AI866782, AI888802, AI186201, BF739152, AI932621, AI379939, BE531047, BF689168, AI262916, AA934750, W60466, AI318103, AA588706, AI354896, AV656354, AW601821, BE744973, AW188567, AW970628, AW188566, AW079392, AA252902, AI472809, AW994447, BE042388, AI368181, AI625947, AA552111, T97710, AA502830, BG259849, AW751488, BF737129, BG222333, BF737107, BG222571, BF916953, BE736954, AW117966, BE871206, AA715308, BE838489, BF835784, BF764625, AW291547, AW087246, AI682601, BF737124, AW074322, BE899333, AI824247, BF914747, BF836557, AI620321, BE672984, BF812178, BF772249, AW389752, BE827597, AW376365, AW362652, AA253308, AW794420, BF882777, U42408.1, U58994.1, AI400709, BE166317, AA635412, AA640681, BF822142, AW974947, AI919122, AW082490, AI469586, AL049715.25, AL445222.9, AC011495.6, AI137852.15, AC022217.5, AC011247.10, AC005077.5, AL096814.26, AL391139.19, AL358976.11, AC009123.6, U91323.1, AC009498.3, AC005255.1, AC003037.1, AC074121.16, AL358777.12, AC006509.15, AC005522.2, AF001549.1, AC007240.2, AL031727.42, AC022425.6, AL049569.13, AC011470.5, AC005015.2, AC022027.5, AC005377.2, AF003473.2, AC011815.7, AC008169.2, AL118520.26, AC008267.6, AP001922.4, AC084864.2, AC002476.1, Z85987.13, AL109976.23, AC010271.6, AC010609.6, AC008569.6, AP001718.1, AC004963.2, AL035088.1, AC090426.1, AC006270.1, AC006449.19, AP001711.1, AL009179.1, AC011465.4, AC020908.6, AC005072.2, AP000251.1, AC005071.2, BF764928, AW959372, AW951170.
	350	545427	1 - 1269	15 - 1283	BF764928, AW959372, AW951170.
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HMSHM14	353	461897	1 - 742	15 - 756	<p>BF184679, BF243347, AW778874, AA523671, AA181455, AA431132, A1560791, BE958209, AA315633, H18045, AV755841, BF030440, BF131135, BG249184, BF670667, AA186625, AA861405, AA663419, AW996056, BE567887, BE865807, AA531308, A1139080, AA843632, W95504, R80694, BF664562, BF977109, A1745163, H98623, C75579, BF666247, AW971769, A1274327, BE565642, A1218737, N93386, BF240785, AA204997, BF215015, BG058583, A1807027, AA493379, BE168171, A1027269, W44792, AA192752, AA772002, BF215015, BG058583, A1807027, AA493379, BE168171, A1285081, AA918748, AA459602, AV682318, W95451, W80402, A1085784, BF106436, AV681563, BE168154, AW604348, W32254, AA311342, A1346231, A1086810, A1348232, BF437332, A1304545, W79010, AW058049, AA157979, A1565637, BF215257, AA205366, A1302529, AW085164, AA432149, H99232, BF690888, A1358223, BE168394, BE932473, W15312, BGI65346, BE835844, AA744881, BE814385, BF131056, AF288991.1, BC005294.1, AF051894.1, A121989.12, AF288992.1, AF267986.1, A132640.4, AL049779.6, AF267983.1, Z62873.1, Z62874.1, AF267984.1, AF267985.1, T54811, T55185, R24125, R27504, R64164, R64278, R76615, R77750, R78101, R80695, H00161, H00199, H01506, H01612, H03815, H11302, H11303, H18029, H18238, H18276, H21844, H21845, H22737, H24019, H40729, H40861, H41003, H39213, H43589, H43591, R93867, H50227, H50262, N25143, N26355, N93005, N93049, W20245, W21356, W21385, W25189, W25405, W44746, W44715, W93846, W93867, W95402, W95407, AA001470, N91043, AA026860, AA026861, AA057539, AA057538, AA088796, AA179997, AA192828.</p>
HMSHS36	354	112769 1	1 - 1388	15 - 1402	<p>AW817008, AW817118, AW951170, AL078634, 24.</p> <p>AV701925, BF793477, AV652861, AV706319, BF733347, AV731015, AA649067, BF217767, AU116940, BG032917, BF811794, BF982391, AU120741, A1133602, BF871285, BF673583, BE620216, A1132952, BE250577, BE797641, AV652798, BF874267, BE883545, BF951636, BF877837, AL133895, BE898175, AU120778, AA577789, AW893125, AW962273, AA720812, AA225638, BE736918, BE153395, AA583363, A1926740, AA601152, BE563291, AA180390, AW845697, AW023095, BG009679, AW962826, BF871283, BF732306, BE616582, AA456928, BF803637, BE385152, AA553442, AA604116, AA503299, BE728115, BF763241, AA584599, A1568660, BF918672, AA808950, N62150, A1761174, AU147985, BF943073, AA418822, BE646483, AW845701, AA081957, A1084217, A1832080, BE379426, AA584606, BE615376, AA593381, AW593396, AA630813, N23657, AA487214, AA601086, AA309271, AA179694, BF755046, AA524729, AA631405, AV730261, AA703315, BE154390, A1052560, BF883829, N23646, AA826146, AA713998, A1940701, BF815608, AA584589, BE790104, AW087334, AA487598, AW939910, A1493725, AA418919, AA779025, BF338817, A1686420, BF001825, BF063736, AA663257, AW872342, BF929662, BF919126, BF919125, A1002286, A1940708, AW845664, AU156101, A1800842, AU148272, AA669412, BE676217, AA584914, A1564481, AA593077, H71269, AW088584, A1479770, BE167158, T07383, AU140348, BF958620, T57745, T57474, T63786, BE141836, AL134317, A1671215, AA910874, AW439349, AA171526, A1968135, BF871286, AA774178, AA353087, AA281350, BE531051, A1858454, H63688, AA076475, AW993580, AW865469,</p>

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HNFTU96	367	460611	1 - 442	15 - 456	BF062478, AC006238.1, AC002551.1, AC024028.10, AC013717.8, AC005529.7, AC008440.8, AC005089.2, AC068533.7, AC002301.1, AC020913.6, AC008569.6, AL138776.10, AC074121.16, AL162426.20, AC005562.1, AC020928.6, AL020997.1, U91321.1, AP001718.1, AC009244.24, AF030453.1, AC007256.5, AL163279.2, AL121579.4, AC006211.1, AC025438.5, AC091118.2, AC002299.1, AC006483.3, AL450263.15, AC006012.2, AC011465.4, AC008635.6, AL122001.32, AL008730.1, AC078962.30, AL162458.10, AL139415.10, AF053356.1, AC020934.7, AL009031.1, AC010319.7, AC068799.14, AC005088.2, AL359091.10, AL137059.20, AC004967.3, AC004491.1, AC005682.2.
HNFTJF07	368	577013	1 - 602	15 - 616	AA487061, AA486615, D78759, AC002091.1, AC004089.25, AC005015.2, AC039056.7, AC006329.5, AC005081.3, AC084693.2, U91323.1, AC002352.1, U82668.1, AL391259.15, AL109897.30.
HNFTJH45	369	410107	1 - 561	15 - 575	AL512382.12.
HNGAK47	370	561488	1 - 1130	15 - 1144	AL390802.2.
HNGAP93	371	520227	1 - 689	15 - 703	AW064091, AC005344.1.
HNGBC07	372	103763 1	1 - 1635	15 - 1649	D80268, AW960553, D80212, D59859, AW966534, AW978661, AV720151, D80253, AV701839, AW952839, AV699447, AW958993, AW973490, AW959597, D59619, AW978634, D80210, D80240, D80366, D59889, AW959799, AV720878, D51423, AW966331, AW949656, D80439, D80219, D57483, AW973482, AW966059, AW966398, AW966342, AW966369, AW973474, AA305409, AW975613, AW966368, AW959136, AV718489, D80166, AW973445, AW964967, C14389, AV719557, AV720616, D51799, AV722801, AV719822, AW966053, AV718692, AW973307, AW973447, AV719324, AV718938, AV718633, AW975605, AW966378, AW975618, AV719913, AW950578, AV718707, AW973488, AW966386, AW960454, AV720211, AV718931, AV720729, AV720731, AW973334, AW966388, AW966397, AW949498, AV723927, AV699866, AW949642, AW973473, AW959202, D81030, D80391, D59787, AW966029, AV718440, AV720028, AW966075, AW966065, AW966022, AW964737, AW960465, D80188, AW966332, AW966399, AW966531, AW958992, AW956397, AV702451, AW966041, D58283, AW966333, AW966013, D59275, D80248, AW960483, D80038, AW962082, D80022, AW949586, C14331, D80024, AW966330, D80195, AW975621, AW978648, AW966385, D59467, D80247, AW959582, AV692290, AV654329.

HNGBT31	373	408334	1 - 625	15 - 639	AV655880, AW965163, D80164, AW973541, AW966030, AW964488, AW949641, AV720791, AW952852, AW966054, AW949645, AV720203, AW964756, AW966050, AV719188, D80043, D80227, AW949657, AW966062, AV719783, D59502, AW959628, AW960473, AW965177, AW959570, AV719468, AV718800, AW965185, AW965197, AW965196, AW973485, AW965184, AV720104, AW965175, AW966400, AW962395, D80196, AV718844, AV720464, AV718770, AV720150, AW966380, AV700229, AV724520, AW959062, AW964477, AW956434, AV699550, AW949500, AW964468, AW949654, AW964532, AV699927, D80251, D59610, C14014, D51060, D51022, AV720533, D81026, D80269, AV726330, AW966032, D80133, D50979, AV750778, D80522, AW966343, D50995, AW973330, AW975623, AW949629, AW949653, AW949631, AW949643, AA514186, AW949618, AW949655, AW966329, D59927, D80157, AV719945, AA305578, C15076, AV718530, AV719632, AV718487, D59653, AV719049, AV723097, AW966043, AW965176, AW973465, AW961136, D80193, AW965158, AW962245, D80045, AW949633, AW959469, AW978642, AW966389, AW960532, AV721386, D51759, AW949646, AW949632, AW949658, AV702365, AA514188, D80302, D80241, AW360811, AW966377, D80378, AW752082, AW753053, AW177440, D51103, AV720035, AW950117, AV699652, AV699746, AW949630, AV700889, AW966023, AV720812, C06015, AV702035, AW966379, AW178893, AL022339.1, AL021937.1, AB028859.1, AF058696.1, AB002449.1, AF271371.1, X67155.2, D34614.1, AB038216.1, D88547.1, D50010. 1.
HNGDG40	374	532617	1 - 506	15 - 520	AA780406, AC003089.1, AC005367. 1.
HNGDJ72	375	532619	1 - 510	15 - 524	AC027689.10.
HNGDU40	376	597526	1 - 1021	15 - 1035	AA613157, C14389, D80043, C15076, D80045, AV718707, C14429, D59787, AV700229, C14014, AV719049, D50979, D59502, AV699669, AV719324, D51250, AV699866, D59467, AV701130, AV701149, AV742720, AW966053, AV719913, AW949656, D80166, D59619, D80210, D80391, D80240, AV723927, AW978634, D80212, AV720211, Z21582, D80196, AV718844, AW949642, AW975621, AV719468, AV744770, D81026, D80219, AV699447, AV719822, D81030, AV718692, AV701004, AW966531, D59859, D51423, AW973307, AW949655, AW949629, D51799, AW960553, D80253, D58283, AV718489, AW949631, AW949643, AV719557, AV720731, AV722801, D80195, D59889, D57483, D80188, AW949653, AV720034, AV719783, AW975618, AV720464, AW959202, AV718800, AV720203, AV719188, D80227, AV718770, AW966062, AV720028, AW959628, AW959570, AV724520, AV720150, D80193, AW965158, AV699550, AW966534, AV699927, AW966054, AW973447, D80949, AV699682, D80022, D59927, D80269, AV718440, AW949645, AW949657, D80038, AV700895, D80366, AV701123, AW959582, AV723097, AW965177, AV721386, AW966013, AW949641, AW949633, AW949632, AW949618, AV700622, AW966043, AV700889, AV720812, AW966050, D59275, AW978661, AW966041, AW949646, AV718681, AW949658, AV700159, D80024, T03269, AW959597, AW960414, C75259, AV718633, D50995, AW975605, AV720791, AW949654, D80378, AW964488, AW960465, AV720654, AV699746.

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HNGEO29	377	532622	1 - 477	15 - 491		
HNGEP09	378	499076	1 - 1028	15 - 1042		AW275971, AL369580, AW576034, AL333692.14, AC004638.1, AC027319.5, AC007011.1, AL354932.26, AK000932.1, AC074121.16, AC019171.4, AL390374.16, AJ400877.1, AL158830.17, AL109897.30, AC008403.6, AL121929.17, AC016025.12, AC002390.1, AL360227.17, AL049709.18, AL353777.18, AC004890.2, AC005098.2, AC005015.2, AL354794.16, AL590762.1, AC020931.5, AP001695.1, AC005052.2, AL121754.18, AC073655.26, AC004166.12, AC005225.2, AC010328.4, AC004876.2, AL133353.6, AP000553.1, AL136418.4, AL139054.1, AC004985.2, AL354873.19, AL121897.32, AC003962.1, AL121972.17, AC011472.7, AC011462.4, AC073316.6, AC079602.15, AL590763.1, AL023575.1, AC007216.2, AC005049.2, AL139095.15, AC005033.1, AD000092.1, AL133453.3, AC011514.3, AC008072.3, AC009123.6, AC006130.1, AC005899.1, AC005800.1, AC016995.4, AL021368.1, AP003439.2, AC005740.1, AC004893.1, AC013726.7, AC007546.5, AL031727.42, AL109984.14, AC005280.3, AC020629.6, AL445490.6, AP000067.1, AC003010.1, AP000506.1, AC004520.1, AL121586.31, AB043547.1, AP000501.1, AC007030.3, AE006467.1, AC012476.8, AL512347.14, AC010203.13, AC004217.1, AL133387.8, AC051619.7, AC002504.1, AL096791.12, AL133347.28, AC004826.3, AC004910.1, AL031663.2, AC006544.19, AC069282.6, AF111168.2, AC005089.2, AC002551.1, AC020908.6, AL022323.7, AC011443.6, AC005914.1, AF001548.1, AC010271.6, AL049569.13, AC079630.18, Z93015.9, AL133246.2, AL356299.16, AC002984.1, AL121658.2, AC006088.1, AC006349.3, AC006125.1, AL096840.25, AC005971.5, AB000882.1, AC005519.3, Z93241.11, AL031447.4, AF196969.1, AC007686.5, AC005041.2, AC016587.7, AC009144.5, AC010618.7, AC009137.6, AL121903.13, AL121903.13, AC024028.10, AL117381.32, AC008392.6, AP003357.2, AL137162.25, AL139317.5, AC004626.1, AC006329.5, AL139396.17, AC007956.5, AC020552.4, AL139352.16, AC003065.1.
HNGHR74	379	553443	1 - 1081	15 - 1095		

HNGIH43	380	410179	1 - 413	15 - 427	AC020644.6.
HNGIJ31	381	519120	1 - 782	15 - 796	AU147901, AA376128, BE562634, AC051619.7, AC020629.6, AL445531.10, AC009412.6, AC005052.2, AC079383.17, AL009172.1, AC016637.6, AK022380.1, AC004032.7, AP000555.1, AC009789.21, Z83851.17, AL359643.27, AC011005.7, AC008521.5, AC008635.6.
HNGIQ46	382	526651	1 - 513	15 - 527	BF960121, AA170832, AA585155, D53447, C14391, AV746334, AI541205, AV745704, AV758830, AW962651, AV755445, AV710906, AI546971, AV713182, AV717678, AV758166, AW950194, AI557808, AV762064, AV763339, AV646672, AV707414, AV756720, AV762898, AV761529, AV711001, AV759474, AV758483, AV763126, AV710831, AC006443.1.
HNGJE50	383	561568	1 - 1023	15 - 1037	
HNGJO57	384	579737	1 - 814	15 - 828	
HNGJP69	385	604891	1 - 971	15 - 985	AL041375, BF525663, H81406, AA599712, AI952574, AC008967.3, AL035407.15, AC007308.13, AC002470.17, AC008626.5, AC010458.5, AC007263.4, AC018809.4, AC002425.1, AE006464.1, AL121594.6, AL031005.1, AC004223.1, AC018642.6, AC009783.9, AC005037.2, AC007546.5, Z82208.1, U52112.1, AC008848.7, AC005079.6, AC006329.5, AC008760.6, AL136131.15, AL121588.24, AL121809.6, AC009229.5, AL353579.17, AC015971.4, AL031774.1, AL033519.42, AP000744.4, AF278704.1, AL031258.12, AC007249.5, AF168787.1, AC005399.19, Z84476.6, AC005080.2, AC008379.6, AC008805.7, U82828.1, AL132657.33, AL109797.18, AC004883.2, AL354864.16, U96629.1, AC083884.6, AC005237.2, Z83838.2, AC002310.1, AF111168.2, AC008543.7, AC002543.1, AC026672.44, AC087240.17, AC010311.8, AL356804.4, AL132780.5, AL161670.4, Z98257.1, AC016769.10, AP001714.1, U95739.1, AC005066.1, AC002395.1, AC011482.4, AC004230.1, AC022211.5, AP000008.1, AL354935.23, AL139415.10, Z82174.2, AP001712.1, AC006023.2, AL590762.1, AC013434.8, AC010485.5, Z98304.1, AC010102.3, AC020552.4, AC006970.6, AC004019.20, AL049759.10, AL050341.18, AL13286.9, AL022316.2, AL049872.3, U63721.1, AL035252.5, AC007676.19, AF053356.1, AL109840.24, AC007316.4, AL356354.10, AL121992.24, AC00517.2, AC003080.1, AL138958.18, AC008044.4, AJ277546.2, AL049868.20, AC012089.13, AC090517.2, AC004491.1, AC083863.2, AC004840.3, AC006026.2, AC008403.6, AC005103.3, AC010618.7, AC00491.1, AC083863.2, AC007050.25, Z97985.16, AC011487.5, AC073492.18, AP000553.1, AL096701.14, AL049830.3, AC007050.25, Z97985.16, AC011487.5, AB015355.1, AC005476.4, AL049569.13, AL132777.4, AC004824.3, AC008521.5, AF047825.1, AL359397.3, AL160256.21, AC079833.4, AC078846.2, AP000211.1, AC007707.13, AC025519.10, D88268.1, AL008730.1, AC000134.14, AC005523.1, AC090527.3, AC008616.6, AL035681.13, AC011455.6.
HNGJT54	386	498272	1 - 1096	15 - 1110	
HNGKN89	387	834857	1 - 911	15 - 925	BF893260, BF893278, BF893425, BF893276, BF893263, AW248583, BF893269, BF893272, BF893265, BF893275, BE856505, AI918922, BF893268, AW794915, AW904504, AW834852, BG231506, AI374775, BF893279, BE149619, BF893568, AU141987, BF997144, AI114816, BF110748, BF893405, BF942210, BF990134, BF942097, AL031674.1, AL356266.9, AL359085.14, AC019210.7,

HNCOM56	388	836064	1 - 942	15 - 956	AC011228.9, AL117329.8, AC004966.2, U82670.2, AC005296.1, AC006992.2, AC000004.1, AP000695.1, AC002299.1, AC008276.4, AC022173.7, AL353734.12, AC025438.5, AC091118.2, AC012558.8, AC005186.1, AL049830.3, AC016395.4, AL138816.12, Z82194.1, AL359645.15, AC006080.1, AC010623.7, AC008430.3, AL163227.2, AC073090.8, AC022416.5, AC005367.1, AC074034.18, AC016138.8, AC003089.1, AL139020.5, AC083874.2, AC009276.9, AL391241.21, AC006327.3, AC009476.3, AL161717.15, AC010163.7, AC026351.28, AC012001.6, AL024507.7, AC005697.1, AC005229.1, AP000696.1, AC020740.5, AC009541.16, AP001726.1, AC004888.1, AP001687.1, AL354802.15, AC024085.5, AC005157.1, AL031778.1, AC025812.11, AC007687.16, AL357149. 13.
HNCOM56	388	836064	1 - 942	15 - 956	AA714124, AC016720.9, AL357075.17, AC008440.8, AF283321.1, AL137792.11, AC006060.1, AC004859.2, AL353668.18, AC004057.1, AL031311. 1.
HNCOM56	389	843515	1 - 728	15 - 742	
HNCOM56	390	892160	1 - 1284	15 - 1298	BF755895, AB011086. 1.
HNCOM56	391	496115	1 - 891	15 - 905	AC005187.1.
HNCOM56	392	520300	1 - 748	15 - 762	AA584924.
HNCOM56	393	520294	1 - 711	15 - 725	
HNCOM56	394	520298	1 - 592	15 - 606	AC006356.3.
HNCOM56	395	531908	1 - 779	15 - 793	AF054925, AC005971.5, AJ009616.3, AL391119. 8.
HNCOM56	396	410114	1 - 412	15 - 426	AP000313.1, AP000193.1, AP000050.1, AP000117.1, AP001718. 1.
HNCOM56	397	135220	1 - 829	15 - 843	AC004613.1.
HNCOM56	398	985880	1 - 2628	15 - 2642	AF535686, AL512658.12, AL356791.9, AC007880. 2.
HNCOM56	399	463568	1 - 685	15 - 699	N68677, BE063506, AA659190, AW063123, AW797598, AW337282, AW074332, BF844388, AA573067, BF844391, AA504679, AA578326, AW499708, BF678990, BF913236, AA749062, AA330576, AC060231.6, AC022027.5, AC023105.7, AL031005.1, AC007221.2, AP002852.3, AP000907.5, AC007541.9, AC020663.1, AC007263.4, AC027124.4, AC004217.1, AC008569.6, AL034379.8, AL022311.5, AF001551.1, AC011472.7, AC012512.7, AC009244.24, AL590763.1, AC018695.6, AL353804.22, AJ295844.1, Z79488.1, AC011114.5, AC011465.4, AC004159.1, AC004805.1, AL356805.5, AC017111.4, AL133477.16, AC005480.3, AL049871.4, AC002288.1, AP000338.2, AL354735.14, AL031120.1, AP000216.1, AC073316.6, AL031597.7, AL138724.12, AL121759.25, AL049793.4, AC018868.4, AC007225.2, AC012085.4, AC007421.12, AL590762.1, AL034377.1, AL139233.8, AC007365.3, AC007298.17, AC002980.1, AC004019.20, AC004477.1, AL139105.17, AC005335.1, AC007365.3, AC007298.17, AC002980.1, AC004019.20, AC004477.1, AL139105.17, AC002045.1, AC005971.5, AL139385.12, AL359552.16, AC011500.7, AC010627.5, AC011445.6, AL109827.8, AC002394.1, AL109963.4, AC020906.6, AC011475.6, AC073542.4, AC006139.1, AC006319.3, AC0090939.1, AC008543.7, AC073347.3, AC010422.7, AC011479.6, AC010878.4, AL450266.9, U73647.1, AL355385.15, AL121808.4, AL160492.5, AF172277.1, AC010768.9,

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HNHFR04	400	646709	I - 1667	15 - 1681	AC012354.8.
HNHFU32	401	562728	I - 593	15 - 607	AI809098, AA758603, AA833679, AW371598, AW371593, AA524974, AC004216. 1.
HNHOD46	402	843488	I - 1341	15 - 1355	AV700498, BG164166, AV700988, AV700545, AL037632, AV762783, BG260565, AV714931, AV760723, AF074667, BF792326, AF034176, BE796439, AW962035, AW976010, AA524604, AV760360, BE541237, AU118837, AV719941, BF678427, AL138265, AW188427, AV733710, AL048626, AU117926, BE909125, AV764490, AU119532, BE067011, AL534817, AV699709, AV686853, AV722030, BE393367, BE538259, AA708751, AT732911, BF346320, AW970915, AA526787, AW131249, AU147226, AV763174, AV760497, BF968141, AV762900, AV759711, AV759356, AV760364, BF307044, AV762902, BF679169, AV759686, AV762779, AW963982, AL042906, AV759684, AV762001, AV759683, AL135377, AV734543, AW408643, AU155227, AV759046, AA601355, BF913258, BE273856, AL044340, AA081138, AL952885, AA584482, AV734401, AL042905, AV722075, AV737621, BF666736, AA211734, AW080062, AV762002, AV761309, AT791227, AW961160, AV763305, AI038990, AV759172, AW102955, AA708108, BF381650, BF828714, AL685198, AL679294, BE066950, AV763952, AA831913, AL679871, AU145521, AL204309, AW151713, AW069670, AA481760, BF892846, AW130036, AV763135, AU140392, AA284247, AW102811, AA722372, AW008212, AU158859, AA640277, U51704, AU155168, BG258140, AW088689, AU155048, AA577824, BE387734, BE867712, AL119123, AW079809, AA601326, BF968610, AA515829, AC008440.8, AC011531.7, AC002302.1, AC027319.5, AC005484.2, AC005972.1, AC010469.7, AL109743.4, AC005077.5, AL035398.19, AC020916.7, AC022211.5, AC002301.1, AC018808.4, AP001711.1, AC008745.6, AC000052.16, AL035587.5, AC008720.6, AC007421.12, AC003101.1, AC034193.4, AC025593.5, AC006511.5, AF04555.1, AC007374.6, AL096814.26, AC005081.3, AL445685.17, AJ400877.1, AC004985.2, AC020558.4, AC009516.19, AC008443.8, AL031447.4, AC006028.3, AL121992.24, AC011465.4, AC008655.6, AC008616.6, AL135928.6, AL513550.9, AL031295.1, AL050335.32, AL049780.4, AC005052.2, AL390060.14, AC011005.7, AP001717.1, AB023049.1, AC007000.2, U82668.1, AC005840.2, AC006530.4, AF111168.2, AC018809.4, AC002477.1, AC011443.6, AC018751.30, AC008622.5, AC023058.17, L78833.1, AC007956.5, Z85986.1, AC072052.6, AL137067.7, AC018635.6, AC002059.3, AC004824.3, AC026172.3, AC018506.4, AP000116.1, AL135927.14, AC007227.3, AL445248.7, AL590763.1, AC005914.1, AP001727.1, AL158207.15, AC010320.9, AP000557.2, AL050318.13, AL139809.16, AC008764.7, AC004882.2, AC007731.14, AJ312686.1,

HNHOG73 HNHPD10 HNTBI57	403	835026	1 - 788	15 - 802	AC008969.5, AC004965.2, AC005037.2, AC000353.27, AC027130.5, AC087590.1, AL513008.14, AC005520.2, AC005088.2, AL133244.1, AC008551.5, AL109976.23, AC011461.4, AL132639.4, AC005089.2, AC010492.7, AC009244.24, AC006930.1, AC007318.4, AC005098.2, AC005399.19, AC005529.7, AC004859.2, AL031584.1, AL160471.5, AL391139.19, AF111169.2, AL133448.4, AL431125.7, AP001670.1, AC011890.4, AC005231.2, AF030453.1, AC010527.5, AL034420.16, AC009247.12, AC010328.4, AC073657.5, AC006120.1, AL117692.5, AP000512.1, AL161452.19, AC022382.3, AL445435.11, AC005722.1, AC005632.2, AL162426.20, AL138721.16, AL163636.6, AL049766.14, AL137792.11, AL391827.18, AC004815.2, AL135901.23, AC020983.7, AC021036.5, AL162724.16, AL590762.1, AC011500.7, AC005736.1, AL022312.7, AP003357.2, AL158830.17, AC004089.25, AC006538.1, AP000212.1, AC008760.6, AL450226.1, AL163249.2, AC009002.5, AL121658.2, AF200465.1, AC025438.5, AC091118.2, AC008736.6, AL121601.13, AC004583.1, AC019205.4, AC010326.6, AC007676.19, AC018638.5, AC008755.6, AF001549.1, AC003109.1, AC009194.8, AL021578.4, AF064861.1, AC011247.10, AL1354808.24, AP001718.1, AL355480.22, AC005015.2, AL079335.29, AC002299.1, AL035086.12, AC005368.1, AL357515.26, AF168787.1, AC074270.25, Z95152.1, AC002470.17, AP001752.1, AC005070.1, AC005332.1, AC005619.1, AC010458.5, AF196779.1, AC006285.11, AC010422.7, AC010463.6, AC004813.2, AC024561.4, AC007097.4, AC005280.3, AL096701.14, AC002985.1, AC007957.36, AL034379.8, AC004257.1, AL033529.25, AL359092.14, Z93023.1, AP001725.1, AL357560.11, AC022261.8, AL031681.16, AC025166.7, AC007999.12, AC005874.3, AF134471.1, AC016025.12, AC006254.10, AC004148.1, U95742.1, AC026464.6, AC011462.4, AC005821.1, AC003110.1, AC009756.9, AC011442.5, U78027.1, AC007619.22, AC010605.4, AL117344.12, AL121975.9, AL136300.22, AC006337.4, AL157838.24, AL158040.13, AC006970.6, AC007488.15, AC000026.3, AC008687.4, AC018720.5, Z84487.2, AL445222.9, AL132855.4, AC006480.3, AL031286.1, AC004906.3, AF196971.1, Z83843.1, AC003043.1.
	404	834927	1 - 926	15 - 940	
	405	570877	1 - 1351	15 - 1365	
					AA584096, BF853760, AL137798.8, AL049569.13, AL137802.7. AL528725, AL517370, AL525337, AL528721, AL517371, BF688870, AL528722, AL528048, BE799446, BF980673, BE735750, BF025756, BG260476, BE799805, BE736521, BF026765, BF688394, BG165306, BE904284, BG105071, BE259792, BE791234, AV706017, BE2666425, BF220099, BE513467, AW009838, BE251361, AW248475, BF984306, BE390525, BF315816, AW248520, AI817167, AW956166, AW149722, BE410046, BG235966, AI188457, BE300532, AW005514, AI124027, BE220534, AI923575, AW471497, AW473722, AI366112, AW104750, AI480234, AA452511, AI696876, AW964824, AL110339, AI804579, BE540036, BE253483, AI740396, AW000853, AI091327, AA452655, AI184221, AA864258, AI192782, BE258188, AI636166, AA402090, AW405644, AI289600, AI299237, AI309629, AI923569, AA450027, BE168977, AA829783, AA505829, BE837825, AW129039, AI802674, BE255478, AA359415, AA373622, AA335352, N27053, BF915342, AA454095, AA852853, AA149479, AA341041, AI523984, BF920668.

HNTCE26	406	116039 5	1 - 2149	15 - 2163	AW517023, AA338985, AA033605, AA359435, AW247428, BE169006, BF108984, AI864722, AW247387, BF111419, AV704626, AW732331, AA825440, BE168970, AI983715, AW878738, BE302856, T24108, AI979211, AW992807, AW863091, AW878649, BE241911, AA852854, BG005253, AW271173, F26257, BE048939, AF104222.1, BC000495.1, BC001947.1, AC006529.1, AB033004. 1.
					BG252201, AV726464, AL529709, BE894106, AV726994, BF970560, BF132059, BF977798, AI703275, AW512938, BG164577, AL529708, AI767521, AI823746, BE220262, AA583438, AI143608, AW468337, AI949854, AV727138, AI620344, AI209187, AI630993, BG007081, AI004986, AI565892, AV715169, AI367983, BF056815, AW394003, R70620, BG007658, AA152183, BF381743, AA565300, AA088574, AA931697, AA995899, AI025252, AA297479, T84083, AW138535, H71679, Z45535, AA297478, AI865989, AA367654, AA150060, AA044326, AW338484, D29436, R24591, AI005551, H00983, H39751, AI669105, T83438, BF091777, AW138127, R21165, BF083909, BE934286, R76620, AA971307, AA745052, AW945769, AI554153, T84151, BE550213, H01724, AW051517, AW373316, AW373313, T89390, BF083903, BE541509, AA180271, AI263504, AF303588.1, AF140242.1, AL133390.7, AF056032. 1.
HNTNC20	407	700627	1 - 1965	15 - 1979	BGI79496, BG254440, AA573206, AI735586, BE326906, AA131359, BF668303, AI522318, AI376670, AW241377, BE350501, AA452451, AA131240, AW242329, AI540415.
HNTNI01	408	135228 5	1 - 2073	15 - 2087	AA447485, AA196688, M86015, AI750365, R13985, BF356780, N28763, AC005028. 1.
HNTSY18	409	104138 3	1 - 1797	15 - 1811	AW470226, BF058886, AI692966, BF058139, BE218656, AI281699, AI241829, AA613450, AC004877.1, AL137162.25, AJ400879.1, AC011551. 3.
HOAAC90	410	130120 2	1 - 628	15 - 642	BF508077.
HOACB38	411	520201	1 - 592	15 - 606	AI439525, AA493464, AI348780, AA653139, AW502688, AA689351, AI887235, AI570067, AW813106, AC069262.24, AC007421.12, AL354735.14, AC004382.1, AC009131.6, AC0090939.1, AP000359.1, Z86090.10, AP001748.1, AL049843.18, AL021391.2, AC015801.25, AL133243.1, AD000092.1, AJ003147.1, AF243527.1, AC004125.1, AC007991.7, AL035086.12, AP001724.1, AC006038.2, AL121886.22, AL133448.4, AC007981.46, AC005207.1, AL359853.18, AC002477.1, AF205588.1, AC013429.12, AL121809.6, AC004980.4, AI229041.1, AC002430.1, AC011475.6, AC009123.6, AC008521.5, AC009506.5, AL139099.2, AF207550.1, AE000661.1, AC006141.2, AC010412.7, AC007899.3, AC005746.1, AP002360.4, AL359751.12, AC011811.42, AL158207.15, AC009144.5, AC007954.7, AL136179.15, AC000353.27, AC010319.7, AC039057.8, AC008044.4, AC005332.1, AC020552.4, AC008569.6, AC007064.27, AL138752.5, AL049830.3, AC015971.4, AC026749.5, AC016637.6, AC008567.4, AL354932.26, AC008891.7, AC011247.10, AL357515.26, AL139316.5, AC018644.6, AC012170.6, U91323.1, AL121992.24, AF258545.2, AL133370.4, AL020997.1, AL163201.2, AC008403.6, AC004816.1, AF168787.1, AC005522.2, AC027319.5, AC007384.3, AP001630.1, AC013717.8, Z95114.19, AL009181.1, AL161436.12, AL133367.4,

					AC021036.5, AC011442.5, AP001711.1, AL356379.10, AL390239.16, AL031281.6, AC012594.7, AE000658.1, AL139353.3, AL050335.32, AF190464.1, AL513008.14, AL353643.10, AC002347.1, AP000513.1, AC020934.7, AL356481.16, AC011455.6, AC018755.3, AC011500.7, AF038458.1, AL137802.7, AC004913.2, AP002852.3, AF001549.1, AC006329.5, AB023049.1, AC005899.1, AL160411.25, AC006315.2, AC009060.7, AL356575.8, AL008718.23, AC005529.7, AL121924.13, AL355343.18, AC004050.1, AC008155.9, AC009086.5, AL117692.5, AC020915.6, AC009116.7, AL020993.1, AC024563.4, AL034420.16, AL109935.39, AL355512.22, AE006462.1, AC020558.4, AC010378.6, AC004000.1, AC009497.3, AF064861.1, AC040160.4, AL139100.9, AC022410.4, AC011445.6, AL133288.12, AC025593.5, AL391987.15, AL034380.26, AL121972.17, AC068640.29, AL135927.14, AL139385.12, Z97056.1, AC000120.1, AC004019.20, AC011742.3.
HOCNF19	412	835049	1 - 1104	15 - 1118	F02459, Z17835, AL264655, BE011950, AV729096, N77968, BF807259, AA658839, AI076081, AW804948, BF987026, AC008078.11, AP002898.1, AL157369.7, AP002392.3, AC010999.6, AL353581.14, AC007383.4, AL133551.13, AL161659.17, AL132772.14, L81392.1, L81391.1, AC005317.1.
HODDF13	413	684307	1 - 816	15 - 830	AC011245.8.
HODDN65	414	520348	1 - 741	15 - 755	BF526964, AV734149, AV760019, AI246796, BE063437, AL135377, AI061313, AA515048, AW274191, AI306232, AL046519, AI251576, AI248050, BF828714, AI311647, AW973992, BF826830, AI207465, AW505253, BF340002, AA303007, AW243793, AA704393, T05118, AI583466, AA504818, T74524, AW855643, AW468048, AA737309, AW732205, AI270177, BF821897, AV755654, AW504168, BG222813, AW965008, AI085242, AW516080, AW500684, AL079734, BE077105, AI380617, AI499954, BE062478, AW237905, AA806804, AA484201, BE148969, AV703187, AI612142, BF724699, AA513551, AA730305, AA515728, AW970940, AI491755, BE301584, AW963444, AI192440, AI053827, AV741663, AA524616, AA515723, AW975626, AA827383, AA678950, BF447461, AW963463, BE138594, AA484366, AI610941, AA829036, BF811714, AW407632, AA569089, AI583252, AA502532, AW502873, BF990660, AW969941, AL046471, BF821009, AC006111.3, AP000553.1, AC004644.1, AL162551.3, AL356481.16, AC005225.2, AC005484.2, AC026230.5, AL354889.14, AC006483.3, AC005229.1, AB044947.1, AL138759.20, AC008102.17, Z84468.1, AC010202.6, AL022311.5, L78810.1, AC004851.2, AL008725.1, AC015550.18, AL359092.14, AF006501.4, AP000075.1, AL022165.1, AC010326.6, AC007151.2, AL031685.18, AC006974.2, AC011530.6, AC005821.1, AC011462.4, Z97876.1, AL049835.3, AL136160.18, AL122001.32, AC004448.2, AC009247.12, AC004686.1, AC010378.6, AC006388.3, AC010255.9, AC009311.3, AC004821.3, Z99716.4, AC005480.3, Z86090.10, AF279660.2, Z98044.13, AL133387.8, AL035462.21, AL049569.13, AC007249.5, AC010363.6, AC002400.1, AL109930.8, AL121675.36, AC018636.4, AC008641.6, AC008974.7, AL121845.20, U63630.3, AC002312.1, AJ003147.1, AC004234.1, AC090527.3, AC009077.7, AL035086.12, AC008072.3, AL031587.3, AC024093.46, AC007620.30, AC091529.1, AL109963.4, AC020901.8, AL133286.9, AC005077.5, AL359091.10, AC009812.17, AL049766.14, AC006077.1, AL022238.1, AL133286.9, AC005077.5, AL359091.10, AC009812.17, AL049766.14, AC006077.1, AL022238.1.

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HODDN92	415	422913	1 - 1925	15 - 1939	
HODDO08	416	790333	1 - 1762	15 - 1776	

					AA910686, BF691447, BF038260, BE613000, BG169000, AA863301, BF897824, AA401453, BE265475, AW339332, BF897816, AA565753, AA51055, AA093151, AA099024, AA699676, AA133969, AA471069, AI693843, BF036820, BF196905, AI911997, AI924160, BF815573, BF897801, AI360309, BF432589, AI813844, AA504750, AI686753, AI806115, AI261776, AI310423, BF940128, AW403869, BE742893, AA134035, AA070230, AW117201, AW026697, AW197588, AW338979, AI123979, BG112376, N98997, AW583508, AA582249, AI654526, BF477527, BE964777, AW628128, AA223526, AA171790, AA971846, H73796, AA171423, AI147095, AA070339, AA693726, AA983737, AA678212, AA070177, AW674690, BF573100, AI085327, AA132700, AW268656, AI923994, AI418621, AI278584, AI248228, AA504652, AA780169, H73783, AA292088, AA693704, AW957393, AI418336, AI740694, AI868945, AA292108, BF964464, AA132811, BE620176, AA100497, AI302064, BF573156, AI039893, AI219311, BE567691, AI192239, AW247578, AI289150, AI564731, H80411, R55471, AA975469, AI494533, AW044091, AI948639, AA863079, W24068, AI061079, BE313730, AI305164, H16101, AI630630, R21932, BF573651, BG057973, AI283354, AI003108, AW999148, H16102, AI268012, R55472, N67966, AA363605, BF691459, BF038622, AI383210, AI350432, AI698241, AA098910, AI122984, AA011640, AI452472, AA070149, H96713, AA046634, BF903467, BG105768, BF762692, N51622, AA303985, AW149938, AA405427, AA121746, AA484923, D20184, H17092, H73784, AA484823, AA379017, AA346687, BF809804, AA371365, AA121692, AA370670, AA248199, AA011641, R05554, D80913, AW884514, AW166740, AA664999, BE961160, AA294828, BF812313, H73797, H80412, R22581, AA046773, BE858968, BE812881, BE775032, D53438, BF511095, BE812879, AA716159, BF038847, AA875914, Z20288, AA345058, R05449, BE789328, AW969365, AW499915, BE898856, BE762335, BE938247, AW956340, BF689788, BF933273, AV685029, AW999572, BE313283, BE962739, AW999933, BF753569, BF753462, BE349202, AL035683.9, AL157838.24, AC007782.20, AC025594.5, AL031681.16, AC008073.4, AC027670.4, AC008745.6, AL096791.12, AL137786.2, AC006449.19, AL031587.3, AL033378. 12.
HODDW40	417	579256	1 - 668	15 - 682	AL915508, AC009116.7, AC004930. 1.
HODEJ32	418	835027	1 - 725	15 - 739	AL671275, Z69713. 2.
HODFN71	419	119486 6	1 - 1112	15 - 1126	
HODGE68	420	834907	1 - 837	15 - 851	AW812930, AI741403, AI193921, AA292663, AW812933, AV707090, BF892766, AA528261, AA513570, BE152032, AW812788, AL139296.4, AL355886.4, AL512449.6, AL360179.8, AC005284.1, AC011246.6, D84394.1, AC034245.4, AC012361.10, AL133373.5, AC027287.20, AL078634.24, AC012039.10, AB020863.1, AL158064.16, AL138758.7, AC034240.4, AL121575.24, AC016045.8, AL157819. 15.
HOEBK34	421	768325	1 - 733	15 - 747	BE463714, AI016683, AW779895, AA632933, BE180615, AL157827.17, AB011792. 1.
HOEBZ89	422	828177	1 - 2506	15 - 2520	BF685342, BG110312, BF685502, BE070832, AW177053, BF815287, BE300677, AW239056, AW750775, BE303001, AW852115, T85313, AW751809, AI783820, AA362844, AW795506,

HOEDB32	423	634994	1 - 1448	15 - 1462	<p>AW377523, T85527, AI090377, AA809125, AW504667, AW813589, AA831426, BF840290, AA533066, AA313025, AI924950, AW963489, AI754421, BF964936, AC010087.3, AL391137.11, AC090051.8, AC026866.8, AC004453.1, AL035089.21, AP000014.2, AC004491.1, AC018926.10, AF196779.1, AC006251.3, AC005670.1, AC030025.1, AP001169.1, AF139813.1, AC008134.3, AP001729.1, AC004228.2, AC006324.3, AL049713.20, AC000120.1, AL163249.2, Z84466.1, AP000501.1, AC008812.7, AL158210.12, AC004701.1, AL139021.6, AL139035.27, AL035460.15, AC020655.10, AC067941.7, AC003015.1, AC006464.3, AC026787.4, AC007006.3, AC023472.4, AC005736.1, Z99716.4, AL157702.10, AL031678.2, AP001858.4, AC016397.5, AL135752.6, AC018832.4, AL133466.22, AC005863.1, AC005837.1, AL162390.9, AC016772.8, AC007344.3, AC016691.10, AC012499.7, AL139350.17, AE000658.1, AF130247.2, AC004849.1, AC019050.4, AC007620.30, AL161731.20, AL049830.3, AC018764.6, AC022468.5, Z97196.1, AP001574.3, AL034402.9, AL158040.13, AC010002.6, AC005288.1, Z97055.1, AC011485.6, AL161935.10, AL356575.8, AL163206.2, AC009736.9, AC021188.6, AL355612.8, AL049795.20, AC004953.1, AC007533.2, AL121586.31, AC019041.8, AC011495.6, AC006312.8, AC068466.4, AC009961.11, AL022576.1, AC012039.10, AC011455.6, AP002812.3, AL451086.6, AL390882.12, AL138758.7, AL139113.21, AL133367.4, AL109743.4, AC005730.1, AC026431.3, AL121582.19, AL117381.32, AC007679.4, AL513008.14, AL162426.20.</p> <p>BE728085, BF525463, AL043598, BE379024, BE729709, BE388931, BF058202, BE389160, BF219910, AA937045, BE888648, BF983683, BF058514, BE729777, BE386542, BE270287, BF220144, BF732488, BF205132, N37022, AI806995, BE302761, AI218926, AI040017, AV700992, BF204637, AW269653, AW664365, BF851636, AA558441, AI971923, BE389935, AI971822, AI984087, BF109553, BE149505, AI371806, BE466285, N63999, AI218921, BE896831, AW105333, AW264122, H97490, BF830445, AW410288, AW856197, AI041603, AW469216, N28797, BE379424, AW662759, AI218000, AI283819, AA789225, AA916425, W67366, AI354311, AW517796, AI343922, AA872912, BE207555, AW410287, AI751344, AI537028, AW379887, AI469495, N23215, AA305895, AV700226, AI399649, AW602751, AI857609, BF832669, BF732356, AW960917, W67367, AI093054, AW132083, AA613324, AI220983, AW241183, AI239424, AW876666, N32087, AI126987, AA722964, BF361409, AI312696, AI193728, H93764, W24695, H11009, AW876671, BF515670, AA166810, AI754948, AA166918, N93890, N93062, H92111, AI208255, AA994700, AA341436, AL043597, AI751345, T58592, R57961, BF929058, AI015141, AA375135, C01839, H14764, AW889983, D12283, BF755440, H06898, AI868297, AA594530, AA303707, AA535409, AA373071, AA885934, AA359174, AI280938, D83887, AW889975, N88528, BE673462, AA341295, BF088497, AA090557, H06857, BF512261, BC000526.1, AL117619.1, AF132000.1, AC003687.1, AL049873.3, AL450324.10.</p>
HOEDE28	424	103648 0	1 - 1621	15 - 1635	<p>BG253644, BE617308, BE908205, BG168469, BE780471, BE962197, BE906067, BF995657, BE909860, AI807170, BF663899, BG119980, BF590292, AW245652, AI925873, AW369626, BE327306, AW835320, AI249748, BE222879, AA829645, N64725, AA921828, BF877027, AI858022,</p>

					AI284125, AW188200, BF343620, BG058575, AW389738, AA308577, AI373933, AW058649, AA827526, AI480003, AI735476, AI088741, BF436493, AW897913, AI417852, AA494550, AW897907, AW338942, BF342403, AA994956, AA405790, AW514957, AI262527, AA494492, AI636409, AI434947, BE049371, BE905083, BG260598, T79610, AA962509, AW167441, AA405896, AW081192, D60231, AI278362, AI554143, AW188080, D81165, BE311649, H30174, AI243196, AA079581, AA740371, BG012145, AA972847, AI306626, AA593832, AW194277, AI351091, AA079481, AA034389, T53345, H28288, AA938450, AA293300, AI976625, BF993722, AA292019, AA258528, AI583396, AI276415, AA328961, H91077, AW736333, AW951949, BF992981, BF836627, H54397, BE041571, AW514433, BF945592, R97080, BF847325, H23972, BE302217, AW591181, R97126, BF945597, R75916, BE162162, AA704066, T53344, R48633, C06420, H91377, H15782, BF946082, N91739, AA323512, H54481, AA634725, AA366052, AI572758, BF943993, BF725666, H15781, AI863929, AI299302, BG010488, BE091179, CI5317, BF992401, BE170194, AI783464, BF992478, AI985743, CI5316, AA534183, AI918432, BE931309, D80793, AA767106, BF089135, AW879610, AI934252, BF089141, BF089154, BF089155, BF941774, AA258372, BG248087, AI383014, AW366744, AA034388, BE702368, AI364001, BF768284, AW601301, BG035284, AW997179, AW873693, BE706964, AW769571, AW245910, AW798864, BG253858, AK027083.1, AK026108.1, AB051532.1, AL390081.1, AL390080.1, AL390082.1, AK026133. 1.
HOEDH84	425	748236	1 - 2065	15 - 2079	BF349611, BE144240, BE144306, AW665086, BE908446, BE673358, BF437802, AI656054, AI741880, AW072783, AA670023, AW205477, AI453672, BF063715, AA603812, BE858966, AA885145, BF091278, AI766417, AA116081, AA043201, BF060900, BE937827, AA583974, AP000577. 4.
HOEFV61	426	833079	1 - 2643	15 - 2657	BF059271, AW173055, AV682872, AI819334, AW593727, AI742596, BE775300, AI825353, AW291804, BE464469, AW291769, AI365110, AI760371, AI339112, AI439770, AI338579, AI091836, AI193821, AA242981, AA836083, AA769364, AI964079, AW978535, AV748559, AA252166, AA873645, T84143, H51863, AI453360, C00241, BF516266, AW628246, AW628281, AA831298, N53279, AW291086, T89383, AB023143.1, AF310105.1, AF229059.1, AF229061.1, AF298548.1, AL117470.1, AF229060.1, AF229062.1, AK026393.1, AK026398.1, AF241727.1, AF241726.1, AC007041. 3.
HOEQ33	427	118446 5	1 - 2396	15 - 2410	AL528504, AU121718, AI820674, T94707, AJ224741.1, Y13341.1, AC079145.3, AJ001047. 1.
HOFTT75	428	911180	1 - 2117	15 - 2131	AL532142, BG260401, BF688316, BF796465, BE907259, BE878185, BF311180, BF182869, BF793219, BF528084, BG164901, BF025894, BF343463, BF027348, BE615276, BF339485, BG251657, BF340866, BE869513, BG168879, BF312304, BF344218, BG035574, BE909308, BF317451, BF346215, BF569244, BF569508, BF341893, BG164819, BG251015, BE876727, BE314260, AU119847, AW732268, AV691326, BF346288, BE907910, BE792057, BF314016, BE386414, BE787546, BF337708, BE384083, BF032872, BF982476, BF313919, BF967499, BE272948, BE878890, BE272586, BE878055, BF853224, BE386215, BG035861, BF686718,

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	429	135237 8	I - 2780	15 - 2794	S78214.1, AB060916.1, AL050146.1, AK026608.1, AB060852.1, AL162062.1, AF125948.1, AK026593.1, BC009341.1, AL136892.1, BC008280.1, AU012755.1, AL137556.1, AF090934.1, Y16645.1, AK026629.1, AF090943.1, AK026528.1, AL050024.1, BC002839.1, AL110196.1, AL512761.1, AB047615.1, AF225424.1, AL359596.1, AL050172.1, AB055366.1, AB060929.1, AL137538.1, AK027164.1, AK026630.1, AL136843.1, AB055303.1, AB060887.1, AK025312.1, BC003684.1, AK025772.1, AK025484.1, AL136586.1, U80742.1, AL137463.1, X65873.1, AF111112.1, AL389982.1, AL162002.1, AF162270.1, AK027113.1, AL122049.1, AK026086.1, AL122050.1, AK025906.1, AL512754.1, AB055374.1, AB050534.1, AL359583.1, AB056421.1, AL136844.1, AK025209.1, AL137271.1, AL512746.1, AB047801.1, AB062938.1, AL133557.1, AL133075.1, Y14314.1, AB049758.1, AL096744.1, AL133077.1, AL133014.1, BC008365.1, AL133113.1, AL137527.1, BC006412.1, AF106862.1, BC006195.1, AB051158.1, AB055361.1, AK026855.1, AL389939.1, AL42082.1, AF183393.1, BC007021.1, AF125949.1, AB055315.1, BC007326.1, AK026533.1, AB060912.1, AL049452.1, AK026504.1, AK026526.1, BC005151.1, AB048953.1, AL137550.1, AB063070.1, AB047904.1, AB056427.1, AL049314.1, AL117583.1.
HOFNC14	429	135237 8	I - 2780	15 - 2794	
HOFND85	430	847424	I - 2034	15 - 2048	BG252755.1, R14839, R14808, AL526882, H17173, BF361444, AI075929, BE883297, AC005754.1, AK024641.1, AF152500.1, AF217750.1, AC025436.2, AC005752.1, AC008688.7, AF152495.1, AF217756.1, AF152493.1, AF217744.1, AF217748.1, AF152489.1, AF152502.2, AF217749.1, AF152496.1, AF217755.1, AF152491.1, AF217746.1, AF152494.1, AF217742.1, AF152490.1, AF217747.1, AF282973.1, AF152497.1, AF217754.1, AF217757.1, AC074130.3, AB046841.1, AY013878.1, AF152501.2, AF152527.1, AF217751.1, AK027526.1, AF152498.1, AF217753.1, AL117449.1, BC001186.1, AF152499.1, AF217752.1, AF152528.1, AF217743.1, AF152492.1, AF217745.1, AK021915.1, AK023190.1, AY013876.1, AF329369.1, AF131761.1.
HOFNY91	431	847425	I - 2392	15 - 2406	AL529530, BE896219, BE905006, BF701370, AV726968, BF697098, D56471, AA398982, D54791, AW952054, D54998, AA137223, D52957, AL529529, BF667411, AV722244, BE539516, AW603940, BG252620, R33682, D53702, AL537902, BG171582, AW752566, BE874188, R79409, BE891332, BE888598, BG180774, AA702285, D52438, AA306169, F00618, M78614, AW965817, BF515338, BF091420, AW847750, AA307191, AA446770, BE785930, AW157201, AW801965, BF031768, T31797, BF031629, AA658190, D52945, BE565940, AA157919, AA136378, AA150656, AW162647, AA282187, AL684319, BE540207, BF028795, H22397, AW847690, AW293605, AL457838, AA938423, T36093, BE878093, T30493, BG251689, BF341242, AW847685, BG169305, BF115649, BG166888, AV727838, BE739764, BF207904, BE738987, AV725549, AV726582, BE865924, BE866601, BE811512, BF028097, BF028440, AA155611, BF030153, AW070701, AA357234, D55509, BF028402, BF208666, BG054885, BF947687, AW997229, BE699329, BG164817, AV727582, AW750879, BG258115, BF446900, BG151519, BF001920, AW300512, AA639868, AA256021, W23904, BE866188, AI925691, R56031, AW379828, H08997, AI904379, AI632020, AW029553, AI950933,

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HOF0C33	432	118615 6	1 - 1655	15 - 1669		AL537523, AL529922, AL531958, AL531931, AL533269, AL531527, AL538370, AL522567, AL533700, AL517522, AL533444, AL532715, AL533022, AL535485, AL537167, AL534487, AL533896, AL535844, AL531994, AL536379, AL532803, AL536823, AL533869, AL532035, AL532179, AL519275, BE740244, AL533860, AL515038, AL533553, AL537985, AL532900, BF343282, AL533210, BF337581, AU117341, AL533099, BE746016, BF337686, BF792204, BF342077, BF525414, BF337225, BF526535, BF339813, BE746023, BF034576, BF725426, BF338260, BF530938, AL037604, BF526573, BF725182, BF526739, BF339663, BF347697, BF526503, BF525581, BF340234, BF338170, BF342084, BF343151, BE745055, BF530924, BF337272, BF343688, BF337021, BF970778, AL537984, BF341103, BF526677, BF338545, BF337395, BF342649, BF526859, BF340775, BF339935, BF526834, BF341477, BF344385, BF340877, BF342826, BF342633, BE736016, BF344578, BF525970, BF342467, BF343650, BF342924, BF340763, BF339538, BE544737, BE908437, BF341003, BF343078, AI207781, BF340051, BF525585, AL522566, BF338449, BE745373, BF337096, BF526010, BF341476, BF967360, BF338852, BF341124, BF338195, BF526745, BF342954, BF339763, BF979514, BE746698, BF339517, BF342360, BF340469, BF339191, BF339887, BF342928, BF341735, BF529338, BE743894, BE908818, BF525856, BF344911, BF338535, BF339332, AL532657, AL531957, BF344107, BF341131, AV723493, BF341782, BF344167, BF339580, BG109919, AW239295, BF528683, BF341918, BF344021, BF343832, BF337793, BF338946, BF338120, AL534486, BF338028, BF340384, BF344732, BF339317, BF341212, BF340817, BF340783, BF343389, AU119892, BF345257, BF340999, BF344258, BF337576, BF344566, BF034877, BF337121, BG170540, BF343271, BF525368, BF339535, BF339226, AV726914, AV727031, BF344177, BF339897, BG163685, AL047863, BF525437, BF525698, BF526269, BF343536, BF343386, BF339198, BF344902, BF526798, BF341498, BF526748, BF341312, AL046091, BF338378, BF342068, BF525844, BF338401, BF526779, BF341154, BF343100, BF342333, BF344867, BF342713, BF526050, BF724784, BF339951, BF340867, BF725357, BF346960, BF342297, BF343041, BF526463, BF341712, BF340168, BF526158, AV691679, BF344920, BE872649, AL519274, BF338219, BF338938, AL533236, BF339512, BF525910, BF339243, BF337714, BF341591, AL041191, BF343646, BG180665, BF525981, BF337030, AL048826, BF340588, AV722425, BF529059, BF526688, AL533699, BF724267, BE745203, BF724793, BF339189, AV684138, AV752186, AV655939, BF343922, BF920088, BF340673, BF340571, BF338384, BF337619, AL043008, BF339850, BF337433, BF526888, BF919959, M64722.1, X14723.1, M25915.1, J02908.1, M74816.1, L00974.1, M63378.1, Y09532.1, M26639.1, M63377. 1.
HOF0C73	433	931871	1 - 1477	15 - 1491		BF195687, AI762843, BF435173, AW167715, BE675436, AI829951, BF195590, AW517368, AI831464, BF110813, BF939079, AW573230, BE747230, AI760936, BF348602, AA418800, AI870845, AI420441, AI377190, BF196297, N32270, AI813507, AI313119, AI472198, AI340272,

AA502942, AI363372, AI806717, AI479956, AA861188, AI073435, AI128897, AI799480, N35138, AA832426, AW753935, AA421515, AW362239, AA258517, AI907351, AA789084, BF924856, H42825, F35882, BF814541, AW409775, AW265004, AA830821, AW089179, AI133741, AA835966, BG029053, BE781369, AI696969, AI565172, AW089006, BE565169, BF527012, AA807088, BE048071, AI567637, AW088899, AI571868, BF725863, BF970263, AI244380, AI119791, BG058039, AW020419, BE964497, AW999906, BE785868, AI400725, AI046463, AI874166, AI922577, AI874151, AW081034, AI620093, AI282903, AI280661, AW193203, AA603709, AI570966, BG260144, BE061389, AI537617, AI919345, BG027628, AW130863, BF915537, AW834355, BF815196, AI648567, BE963918, BF915208, BE072233, AI952302, AI805638, AI366549, AI636719, AI539153, BE964767, AW085786, BE538466, BF904180, BE172499, BE963286, AI036638, AI857760, AA568405, AI611743, AI689420, AW083804, AI696626, AI633477, AV757067, AI589993, AI365256, T99953, BG105895, AL038505, BF814449, AW022682, BE393551, AA464646, AI963062, BF817746, AI886055, AI472536, AI677797, AW999599, AF009923, AI, AI09840.24, AC010102.3, BC008142, AI, AF136273, AI, AF032906, AI, AF136275, AI, AI389978, AI, BC004874, AI, AK024538, AI, AK025383, AI, AK000137, AI, AB063079, AI, AL359600, AI, BC004265, AI, AK026624, AI, BC001349, AI, AF262032, AI, AB063074, AI, AF188698, AI, BC007355, AI, AK000421, AI, AF069506, AI, BC009253, AI, BC008382, AI, BC004908, AI, AL359620, AI, AK027868, AI, BC007456, AI, J05032, AI, AF090886, AI, AL137292, AI, BC002454, AI, AB063008, AI, BC001045, AI, AL133016, AI, AF078844, AI, BC004529, AI, BC007255, AI, BC008488, AI, AF125949, AI, BC000556, AI, BC008893, AI, AL080060, AI, AL049382, AI, BC007534, AI, AL389935, AI, AB019565, AI, BC005007, AI, AK025708, AI, AL162006, AI, U42031, AI, AL096751, AI, BC007389, AI, AL136692, AI, AL050277, AI, AL512719, AI, AF067420, AI, BC005678, AI, AK024588, AI, BC003650, AI, AK024601, AI, AL122111, AI, AB048975, AI, AK000647, AI, BC003548, AI, AL137521, AI, U91329, AI, AL137665, AI, AL117432, AI, AF271350, AI, AL133104, AI, AL110196, AI, AK000445, AI, AF218014, AI, BC006164, AI, AK026522, AI, AK026626, AI, AL133081, AI, AK025958, AI, AF217987, AI, AB048974, AI, BC000316, AI, AK027164, AI, AL117457, AI, AB062978, AI, AL137300, AI, AB056768, AI, U77594, AI, U39656, AI, BC004370, AI, AB049848, AI, AK000652, AI, AL512754, AI, AB056427, AI, AB060211, AI, BC008785, AI, BC003682, AI, BC008417, AI, AK000753, AI, BC008282, AI, AL133014, AI, BC006201, AI, S76508, AI, AF081197, AI, AF081195, AI, BC003687, AI, AF239683, AI, AF348209, AI, AL353625, AI, AL117648, AI, AL137429, AI, AK026533, AI, AK026504, AI, BC006508, AI, AL512761, AI, AF305835, AI, AB049758, AI, AF217991, AI, AL122121, AI, BC006133, AI, BC005835, AI, AF091084, AI, AF162270, AI, AF159141, AI, AK026642, AI, AB060905, AI, AB056421, AI, AK024974, AI, AK027081, M92439, AI, AL390167, AI, AL080086, AI, AL080074, AI, BC000550, AI, BC002647, AI, AB063070, AI, AK000432, AI, BC003602, AI, AB050510, AI, BC007391, AI, BC008673, AI, AK026526, AI, AB060852, AI, AF303581, AI, AF178432, AI, AL136586, AI, AL389939, AI, AJ006417, AI, AK026353, AI, AB047615, AI, AB047897, AI, BC008040, AI, BC008280, AI, AK025573, AI, AF219137, AI, AL110221, AI, BC007998, AI, AL442072, AI, AL137527, AI, AL050393, AI, AK000450, AI, BC000348, AI, AK026591, AI, AL136790, AI, AC006451, AI, AF012536, AI, AL049460, AI, BC007280, AI, AF218031, AI,					
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HOGAW62	434	579891	1 - 557	15 - 571		AL157828, AL519145, AL531212, BE314599, AL527137, AL516077, AL521270, AL528374, AL517829, AL527760, BE410195, BF207279, BE894391, BE275383, BF344492, BE545217, BG116866, BE869193, BE910148, AL527158, BE905116, BE906070, BE539313, AL521271, BE544985, AW370647, AI080486, BE272322, AW129545, AW370565, AW370566, AW370569, AW370587, AW370585, AW370632, BF036759, BF111664, AW370635, BF036029, AV751399, AW370628, BF793770, BE161918, BE644987, BE513159, AL516078, AW952389, AA573800, AW361708, AW370597, BF793672, AW361545, AW370593, AI884757, BE905445, BE644790, AW370591, BG032275, BE545897, BF795549, BE781323, AW370583, AI751504, BE390637, AW370629, AW370626, BF307320, BF312112, BE616107, AW874541, AA599271, AA305125, BF305377, BF305746, BE304395, AI670082, BE548571, AI201054, AA044111, BF345456, AW387317, BF027143, AA410751, AW370645, AI979204, BE259925, AI687237, AW167891, BE385822, BE312740, AI828402, AI907591, AI819020, AW631188, BE298820, AA044057, AW103037, AA523198, BE298172, AA878137, AI754894, AI016005, AW662228, AI375007, AW130175, BF346901, BE388396, BF345509, AI690636, BE869078, AW440908, AW370586, AI907608, BF035998, BE293025, AI285110, BE139500, AI342760, AI862740, BE260090, BF761781, BF882238, AI028777, BF882332, BE877444, AA947042, AA032233, AW170149, BE893722, AW370624, AW273212, AI907602, BF310543, AA878164, BF763648, AI907600, AA618599, AA935855, AI074254, T69117, AI432547, AW370603, AI350390, AW510421, AA045976, BE737019, Z44367, AI613194, AA309604, AA846754, AW512536, T31182, BE615661, BE296557, AW370571, AI803040, C01877, AW516417, BE294829, AI241142, AA551200, AA506057, BF941946, AI805655, BF761823, BF083958, AI355466, AI751505, AA781304, BF875067, AA912801, AA620419, AA305077, Z40301, AW129402, AA806679, H83225, BE082695, BE263189, AI948632, BE938441, AW405902, AW370600, AL449482, AV693457, BG151231, BF879463, H25231, AI597749, BE244231, BF761766, AV688978, AA329345, T30732, AI420548, AA496987, AA852486, BE019097,
HOGCK20	435	745445	1 - 2073	15 - 2087		

					BF881592, AI968145, AW197407, AW374690, R18126, AA336532, AW952473, BF304701, AA852434, AI906426, AW023694, H82992, BF836250, BF807559, AA852485, AA852433, AA336533, AI368088, BF337774, AW881423, AA306344, BE773038, AI739470, AI274423, H46420, AI268055, AW512535, AI364223, AI969087, AW881344, AI673433, AI933569, BE076501, AI590377, AA580549, AI371192, T31989, BE218679, BE764975, BF950840, D59206, AA862206, BE074269, BF110288, AW028921, BF821577, AW793552, F23516, AA323541, AI691101, BF359554, AF132940.1, AI121742.1, AB057724.1, AF314058.1, AL021578.4, AF058295.1, W32805.
HOGCK63	436	895880	1 - 1395	15 - 1409	AL515915, AL519637, AL516502, AL530378, AL534541, AL527244, BF206279, BE563468, BE894600, BF528095, BE734337, BE261458, BE547607, BF207129, BE018805, BE258538, AA314355, BF966160, BE259017, AI878986, BF527510, AW961100, BF218016, BF805533, BE935456, BE273252, BE935565, BE379416, BF689497, BE615561, BF805135, BG250649, BF805538, BG111006, W00898, BE394407, BF805707, BE543852, BE935562, BE538668, BG012784, BE797749, BE870449, AA340663, AA337437, BF093795, BE617246, BE168598, BF827571, BF827568, H74337, H26577, R13677, H15188, BF827533, BE935468, BF920853, BF183200, BE617395, BG025917, BF769129, W52074, W00927, BE887136, N75733, BG253784, AA033549, BE938018, BF378489, BF531045, BE935512, AW389834, AW579752, BF984332, BE408926, N91321, T97551, AL530377, BF965806, BG112290, AL515914, BG104543, AW840975, AW840976, BG120271, BF808337, BE617147, BE174138, BF803235, N39949, BF852997, BF852999, AA037261, AA827575, T83003, N77103, BG178316, BF807890, BF980427, AW581002, BE311929, BE887785, BE892497, BE935460, BE935465, BF207193, AK027879.1, BC008732.1, BC001230.1, AF151835. 1.
HOGCS52	437	919898	1 - 2557	15 - 2571	AL530487, BE745421, BF330206, BE744240, BE732555, BE560832, BE728102, BE734494, BF340173, BE900928, BE899085, BG171027, BE407847, BF339012, BE391461, BE005931, BE387398, BE392364, AW962475, BF345275, BE269190, BE280532, BE870859, AI569503, BE392132, AL530895, BE908923, AA521235, BE295971, AW262804, AI264216, BE018918, BE890434, BE005979, BF961405, BF343159, BE715414, BE542338, BF792605, BE514659, AI636351, AI859499, AI744758, AA758222, BE675736, BF124910, AI126826, AW024550, BF530317, AA594600, AI567104, AI935268, BG149675, AW510761, AI280100, BG231713, AI363344, BE782378, BE245842, BF896674, N72581, AW082737, BF348228, AI291530, AI633705, AA483476, AI376854, AA862073, AI439117, AW360876, AA774640, BG006132, AI459751, BE504207, AW300087, AI673280, AI885032, AA405342, BE218474, BF896671, AI022088, AA788862, AW341140, AI168484, AA703032, AA631579, BF376297, AW026262, AA733166, AA878000, AA456364, AI693928, BE208332, AI377769, BE295604, T47288, AA393265, BF995787, H80493, AW261896, AA682322, AI189548, AW574867, AA224519, BE828754, BE828767, BG149772, AA523423, AA398668, AW264368, AW276800, AI239429, C01609, N76973, BE294075, BF338783, BG261025, H81411, AA813297, AW263725, BF594376, BF088543, AW392277, AI362740, BE770083, BE828760, AW403980, BF309314, R71977, AA574078, AI949151, AI762166, H00206, AI360375, BE828785, BE089517, BF753501, W46600, N55486, BE828765, BE828818, BG011135, BE828755,

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HOHBB49	438	833080	1 - 3066	15 - 3080	<p>AW176451, AV763354, AV764307, AI284640, AV760937, AW193265, AV762111, AV764241, AL046409, AI963720, AI270117, AV710066, BF668217, AV759274, AV763255, AV761786, AV762139, AI281881, AV760571, AA577906, AL038705, AV740801, AW406447, AV761745, AI345654, AW270382, BE253048, AA483223, AA491814, AI431303, AA526787, AV762050, AV763971, AI334443, BF677892, AI801482, AF330238, AW419262, AA491284, AA468022, AW500125, AV762098, AV759382, AW274346, AI350211, BF347791, BF347740, AA610491, AV762395, AI613280, AW517377, AV761925, AW502975, BE394054, AA490183, AV763122, AW662543, AV735370, AI619997, BE150580, BE047069, AV761294, BE139146, AV759362, AL041690, BF475381, BE160727, AA523837, BF854876, AV759204, BF337291, BF915247, AI654525, AA581903, BE350772, W79504, AA623002, AW963497, AA610493, BF915628, AW503666, AW960468, AA584167, AI799642, AV762009, F36273, AI732865, AI355206, BF915722, AL121235, AV762826, AA533725, AL048925, AV760777, AW276827, AW438643, AW238278, BG249643, BF793766, AV763847, BF915839, AI061334, AW504669, AI821271, AV764578, AA503015, AA613203, AI499938, AI754658, AI561060, AW410400, AA469451, AV761362, AW273218, AA806796, BE672637, AW265393, AA101689, AV761106, AI754336, W47183, BG104686, AA780515, AV728632, BE350475, AI375710, AA493471, AA507824, AI811687, AV728928, AW473163, AV728425, AA613232, AA587604, AA653618, AW070892, AL044940, AW167372, BG059450, AI860013, AI149478, AL042420, AA446657, BF991286, AW072923, BF940837, AW956640, BF883982, AV759239, AW769399, AA630925, AV760704, AA525824, BF697673, AV725423, AI744995, AI085719, AA665021, AV761489, AV762154, AA578997, AI688846, AV762505, BF970654, AV760624, AA682912, AW962175, BE072475, AV710774, AW500353, AW979060, BF592311, AI732120, AW731867, AV658631, AI860020, AW088202, AA599920, AW193432, AI133164, AI246119, AI471481, AI368745, H72402, AV760042, AI610159, AW513362, AI345681, AI345675, BF592200, BE042649, AA834792, AW956641, AA984708,</p>

HOHBC68	439	603968	1 - 1823	15 - 1837	AC011471.6, AF135028.1, AC006057.5, AL135940.11, AL031391.1, AL023575.1, AC004534.1, AC003080.1, AC009179.17, AC007240.2, AL022328.21, AL445209.4, AC007191.1, AW889450, BF799811, AW961831, AA309158, AA309202, BG005728, BF998803, AW888368, AI904188, AK000465.1, AB033025.1, AL109667.1.
HOHBY12	440	625973	1 - 1174	15 - 1188	AL566933, BF916217, BF991303, AB051431.1, AL022339.1, AL021937.1.
HOHBY44	441	873264	1 - 3355	15 - 3369	AW604409, AI037867, AW604404, AW368603, AW151676, AW383192, BE696058, BE927254, BF431876, AI753734, AI754387, BE696055, AW044602, AW383224, AI041650, AW383194, AI750595, AW383164, AI884505, W52686, AW069006, BG256681, AW842507, AW956164, AI750594, AA600082, AW078795, AI753050, AI802788, AW190902, AI750578, AW957491, BF055368, AI041803, AI621183, AW631119, AI750577, AW383125, BF215485, AA599801, AW087935, N31127, BE696060, W51909, AI087351, W47324, AA071381, W48619, AA670070, W48852, N35377, AI752124, AI090390, W42791, W47325, N28395, N28453, BE693590, BE693587, AI085102, AI678451, AA545734, W42884, AA373348, AI302125, AI910477, H80042, AA071138, AA669811, AW361415, AW069430, AA788723, AW069485, AW853798, AI940729, AI754608, AW580737, AA376403, BF508389, AA373673, H99469, AA373544, AW473621, BF881941, AI888605, AA373014, AI940705, AA373975, N27040, C01826, AA373298, AA112124, AA084001, BE140157, AI940795, AA372833, BE140143, BE140150, AW005943, BE140098, BE140177, BE140175, BE140179, BE140161, BE140145, BE140148, BE140155, BE140167, BE140163, BE140147, BE140158, BE140149, BE140176, BE140107, BE140146, BE140152, BE140144, BE140099, BE140102, BE140166, BE140116, BE140156, BE140173, BE933516, BE140174, BE140104, AW239511, BG108248, BE140160, BE140171, BE140105, AI521673, BE140109, BE140164, BE140172, AW806615, BF109257, AW138508, BF217716, BE140108, AI932934, BE140103, AA373557, BE140153, BE140117, AA344024, W25447, AW806557, AI537571, BE140162, C01953, AI476777, AW583945, AF110137.2, AL359060.1, AL359059.1, AF154054.1, AB032372.1, AF043800.1.
HOHCC74	442	547977	1 - 544	15 - 558	BF217791, AV747014, T66046, AA676735, F12094, AL043886, T65277, AC018755.3, D50419.1.
HOHCH55	443	827481	1 - 2485	15 - 2499	AW967050, BF793252, AA150407, AI889756, AW068908, AI539422, AI189000, AA149419, AA047109, AW304902, AI750990, AI123024, AA317245, AI752854, AI095919, AI984090, AI679980, AI954496, AA047265, BF749346, AW068311, AA136657, AA417383, AA446268, BE763257, AA136596, AA852682, BG222753, AA150286, AA417352, N52533, N52541, AA149305, AI129506, AA723730, BF987955, C01867, AA445992, BF928215, AF072752.1, AB008375.1, AL160153.11, AL355807.11, AL139800.10, AL359052.1.
HONAH29	444	129992 8	1 - 1609	15 - 1623	BE877138, BE541324, AW961713, BF130173, AA446931, BF982552, AI750643, AW298762, BF678790, W44974, AI752977, H70832, BE865917, AA279599, AA661554, AA362887, AA347452, AW955588, T55597, AA443355, W42674, AA452666, BG168559, AA774309, AA828840, AW021674, AI124558, AW304932, AV763460, BF915849, AW576388, AV759517, AW023975, AW403177, BF817511, AA702637, AW237905, AW839858, AW409626, AA557945, AA661583, BF815277.

AL039436, AI640905, AA584360, AA282951, AF147776, AI444575, AA557911, AL042667, AL042670, AI251024, AF702049, AA468458, AA604149, AW069273, AI254267, R83585, AV758849, F25759, AI439525, F35374, AA604601, AI753969, AI46789, BG059139, AW265468, AW615441, W04133, AA167656, BE886321, AW514844, AI798521, AW516058, AV720223, BG180320, AI158382, AI921350, AI121039, AI912867, AA312920, AW975239, AI253356, AA828613, AI358505, AW409621, AI282479, AW270385, AV728973, BE062545, AU152824, AI308529, BF739035, AW029626, AW327673, AA218874, AA218757, AW410844, AI744963, AA847341, BF901147, AU151031, H84028, BE045167, AV719881, AV755245, AV729090, AW968188, AU150590, AU154339, AI888050, AI554399, AA228268, BE139139, AV718593, T03576, AI250552, AI251034, AI254770, AI284543, BF882222, AI581119, AU147301, AA169245, AU152669, BE260841, AI064968, AI860648, AW861117, AA835702, AA663579, AU149150, AI281622, AK000738.1, BC005206.1, AC007285.3, AC006435.7, AC002070.1, AL356575.8, AC010150.3, AL157829.24, AC007011.1, AL137792.11, AL139316.5, AC067722.21, AP000689.1, DI4872.1, AF243527.1, AL034420.16, AC087879.8, AC018828.3, AL138724.12, AC022383.3, AB003151.1, AC004067.1, AC020916.7, AC026464.6, AL133174.15, AL450226.1, AL139195.4, AC007226.3, AL121890.34, AC009948.3, AC083863.2, AC022384.4, AP001725.1, AL121594.6, AL121893.21, AC073657.5, AC005245.1, AL096819.17, AC091394.2, AL135858.3, AC008745.6, AC010654.8, AL035684.25, AL109743.4, AC010742.4, AF084941.1, AL138756.23, AL121886.22, L78833.1, AC011464.5, AL136137.15, AC005785.1, AC007240.2, AL133453.3, AC007688.15, AC020552.4, AL031433.4, AC005399.19, AL355543.13, AC002350.1, AC002465.1, AJ003147.1, AC002558.1, AL353804.22, AF207550.1, AC004814.2, AC007151.2, AL136418.4, AL139054.1, AL160471.5, AL035420.15, AC010271.6, AC006468.9, AE006463.1, AL353748.13, AL161871.6, AC007375.6, AB023048.1, AC005666.1, AC004659.1, AC005412.6, AC008739.5, AL022320.23, AC084864.2, AL163612.5, AC005899.1, AC010139.4, AC008764.7, AC006486.1, AC011480.3, AC005306.2, AL391647.16, AC034193.4, AL133246.2, AL008734.10, AL135839.15, AC010282.5, AL121712.27, AC010205.5, AJ011930.1, AC009131.6, AL117336.22, AC009506.5, AL138759.20, AC015937.7, AL445489.10, AL008731.1, AC008784.6, AC004223.1, AC015801.25, AL133371.3, AC034235.4, AC010422.7, AL022727.1, AL352978.6, AC010789.9, AC011816.17, AC007956.5, AC004089.25, AC003041.1, AC090937.1, AC018808.4, AC006057.5, AL358174.12, AL121933.15, AC010316.6, AC005837.1, AL445263.6, AL050341.18, AP000107.1, AC011811.42, AL031311.1, AC004765.2, AL096701.14, AL133477.16, AL109952.15, AL160037.17, AL135838.5, L44140.1, AC008672.5, AC002425.1, AC011465.4, AL122004.17, AC004824.3, AL136305.14, AL133241.3, AC079907.25, AC019205.4, AC005516.1, AC004812.1, AC005911.6, Z98884.11, AC008626.5, AC009314.4, AL117329.8, AC005747.1, AC006385.3, AC005907.1, AL354864.16, AC005102.1, AC011495.6, AC010326.6, AC006463.3, AL121928.13, AL450339.5, AL021707.2, AC010530.7, AL136228.8, AC024561.4, AC009060.7, AC011450.4, AL096712.20, AC005330.2, AC002477.1, AC006344.2, AL109825.23, AL353682.11, AC007900.5, AL109923.29, AC005365.1, AP000502.1, AL035588.21, AK000832.1,					
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HOSDI25	445	854234	1 - 2200	15 - 2214		AL521533, BF966564, BG109192, BE621548, BG259805, BF666690, BF667661, BF185318, BF666019, BE621125, AL43432, AW963800, BE883279, BF028488, BF667980, BF196902, BF111775, BF667265, BF664922, BF966437, BF667218, AL277896, BF028500, AL401346, BF696865, BF698781, BG169528, BF696312, AW338135, AL280253, AA873621, AL435513, BE552077, BF699387, BF055949, BF697521, BE542555, AL277959, AA121788, AJ961880, AW969937, BF478121, AW338124, AA528626, AW367010, R76478, AA101422, T62844, AI918990, BE167397, W72961, AA876737, R28131, BE176581, AA375127, BF332407, AL365181, W73131, T62693, W21429, N92911, BF570557, AI077290, AA127501, R66340, AI926197, C00153, AA813575, R28517, AL580500, AL222072, AI033269, AA758476, W86851, AV661704, AV725920, AV728997, AV704234, AV726624, AV655280, AV729378, AV708992, AV727787, AV709407, AV654908, AV660608, AV652001, AV656903, AV707541, AV706854, AV702117, AV726738, AV728733, AV708834, AV687035, AV697196, AV708704, AV659322, AV656478, AV698545, AV709314, AV708381, AV660728, AV691080, AV651955, AV703169, AV728518, AW952409, AV709660, AV729220, AV696866, AV726816, AV695545, AV656283, AV708025, AV707933, AV684604, AV708980, AV692691, AV701914, AV705159, AV702516, AV693523, AV726103, AV727029, AV725826, AV725134, AV705280, AV702994, AV683272, AV697288, AV652156, AV728670, AV708723, AV729263, AV707510, AV699089, AV658863, AV701560, AV727776, AV698609, AV696106, AV706744, AV708438, AW951263, AV689111, AV728157, AV708109, AV692345, AV704553, AV683443, AV708893, AV659536, AV706219, AV658275, AV705693, AW960720, AV686064, AV705632, AV706721, AV701067, AV709604, AV704955, AV701707, AV707753, AV706089, AV704269, AV703495, AV702021, AV706677, AW960326, AV709869, AV656256, AV687909, AW954031, AV702832, AV708622, AV729259, AV726784, AV702833, AV707296, AV707767, AW958647, AV654896, AV645906, AV728806, AV652617, AV703599, AV727990, AV701580, AV708004, AV727003, AV703970, AV727526, AV727799, AV728471, AV703472, AV702147, AV686060, AV726156, AV649758, AV706342, AV702266, AV729189, AW953965, AV696931, AV698429, AV692972, AV685688, AV689800, AV693005, AV709390, AW953787, AW952414, AV722222, AV645936, AW955653, AV706185, AV684075, AW951618, AV658332, AV703168,

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HOSEGS1	446	545809	1 - 576	15 - 590	AA181348, AW968493, A1651957, BF593221, AU157244, AA459376, AI078788, AU144318, AI270699, AW605061, AI082584, AI522177, BE645867, AU149785, AA09435, AV716472, AW139763, N52810, AA610587, BE937915, AA765149, AW385335, BE709275, AA774278, AL538336, AK002014.1, AK021520.1, AK001369.1.
HOSFDS8	447	614040	1 - 2513	15 - 2527	AL517202, AL517203, AW957146, BG116418, BF038478, AI563954, AU132232, AA932901, AI755091, AI831671, BE889854, AU127679, BE891799, AI582904, AI038368, BE246025, BG177748, BE906332, BE277910, BF982210, BE276343, AI633334, BE891988, AI954440, AI687563, BF984413, AW956931, AI565064, AI879207, AW778725, AI472032, AI924693, BF972236, BE889752, AV753606, BE536916, BE269039, BF196580, AA165526, AI248179, BF060729, BF308455, BE539211, AV734590, AA165570, AI219806, AI803270, BF027703, AI433120, AA780394, AW593783, AA305509, BE887807, BF032636, AA314159, AA745078, BE677439, AU150180, AI525645, AL046195, AW388378, AA740296, BE858748, AA745958, AV753692, BE934649, AI879591, BE671082, AW390682, AI091788, AW118905, AW407201, AI521298, BE327080, AA993868, BE550016, N39180, AI249054, BE301992, AI147071, AI137129, AA939319, AA593391, AI751805, N62852, AW473172, AA513491, AA630359, T09181, AA824241, H40891, AI570848, N77759, AA169832, BF948867, H18116, AW875628, N48472, AI168762, AI984827, AA312180, T15583, AW263215, H07053, AA644510, BE018377, H12907, N39112, AI751806, AI538630, AI478724, AI364661, R54299, AA137058, AW571962, AW137978, AA236150, BF512413, T31959, T09180, AA165129, AW965437, N49188, AI393653, T31501, AI889542, AA507842, R51911, AW273523, AI807100, AV695683, AW085260, T36296, AA236118, AI091951, H50337, AA493467, AW664638, AA304893, AW150373, AW519322, BF901925, AW079446, AA029150, N73896, BF744173, AA878611, H07054, AA676446, H05492, AA332663, AI167495, AA361172, AI240673, AA337044, T05940, T34466, AW474105, AW388354, N45253, AI460248, BF750384, AI954456, T16557, T31824, BE763619, AI499330, AA385497, N84723, BE842309, AW387927, AW388264, H28059, N50243, AW387979, D56528, AA169652, AL036975, AL043667, BF375439, AI908550, AA029027, AW387992, W03958, BE778418, AA484014, BF992834, AA019284, AF105227.1, Y10387.1, AF033026.1, AF016496.1, U53447.1, AC004045.1, AF097721.1, AF097719.1, AF097712.1, AF097720.1, AF097717.1, AF097713.1, AF097718.1, AF097714.1, AF097711.1, AF097715.1, AF097716.1, AF097710.1.
HOUQC17	448	429229	1 - 4698	15 - 4712	AI810627, BF344199, BG056542, BG118486, AI126019, BE784908, AW954313, W07142, AA133346, BE047207, AV700629, AW163200, AI692832, BF589805, AW195344, AI755040, AW964293, AI890478, BE856510, BF370410, AW168050, AI985641, AI926525, AI369060, AI654583, AI571069, AU158513, AW167394, AI129429, BF244275, AW474740, AI887177, BF083290, AA993528, N91530, AI148739, BE925407, AW001362, AA022464, BF203604, AW194129, BF590332, AI144408,

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HOUDK26	449	565393	1 - 1037	15 - 1051	
HOVCA92	450	527644	1 - 693	15 - 707	
HPASA81	451	135238 2	1 - 1931	15 - 1945	
HPBCU51	452	411080	1 - 585	15 - 599	
HPDDC77	453	130689 9	1 - 964	15 - 978	

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HPDWP28	454	109460 9	1 - 514	15 - 528	AI394037, AW303979, AW293101, A1827868, AA010190, BF001923, AW006972, A1809548, AW138946, BF476527, BF084139, AK025743.1, AF000067.1.
HPEAD48	455	520367	1 - 611	15 - 625	AW964468, D80045, AW966389, AW949645, AW966330, AW949642, AW964532, AW965158, AW949643, AV738340, AV744012, AW975618, AV744690, AW366296, AV702035, AV723097, C14389, AV724520, AV742048, AW962395, D51799, AW964488, AV719468, D59502, AW375405, D80195, AV720791, AA305578, AW966050, AW965185, AW965197, AW959597, AV742732, AV718800, D80164, AV742050, AW966053, AW966013, AW949658, AW975621, AW966054, AV719783, AW966534, AV720464, A1905856, AW960465, AW949654, AV705134, AW966022, AW966075, AW966041, C15076, AW966065, AW973541, D80038, AW978648, AW959062, AV719324, AV718440, AV720028, AW975613, D59467, AW965196, AW965184, AW965175, D59275, AV718770, AW966030, AV719188, D80227, AW964477, AW966062, AW949641, AW949646, AW959570, AW966029, AV718707, AV705869, AV699927, AW973334, AW966531, AW978634, AW956434, D58283, D80022, AW965163, D80166, AW959799, AW966059, D80193, AW960473, D59859, D59619, D80210, D80391, AV704180, AW960553, D80240, C14331, AW973474, AV719822, AV718692, D59787, D51423, AW973488, AW978661, AV720211, AV718844, D81030, D80253, AV718489, AV720203, AW964756, AW973307, D80043, AV723927, AW177440, AV718938, AW949656, AV718633, AW959628, AW965177, AW975605, AW973485, AV718931, AV720878, AV719557, AV720731, AW973482, AV699447, AW958992, AW958993, AV722801, AW959136, AV699550, AW962082, D80269, AW959202, AV720812, D80212, D80196, AW949657, D80188, D80024, D50979, D80219, AV706147, AW753067, D80268, AW966043, AW949655, AW959582, D59927, D59610, AV720533, D57483, AA305409, AV719628, D80378, D80366, AV741220, D51022, AV706229, AW973330, AW962245, AV721386, AW973447, D59889, D50995, AA514188, D81026, AV727978, AW960454, AW949653, AW949631, AW949618, AW959469, AW964737, AW966032, AV720150, AW960532, AW956397, AW949629, D51060, AW949633, AW949632, AV700889, AV699866, AV701123, C14429, AW973490, AW752082, AV726812, AW753053, AW965176, AW966023, D80241, AW177501, AW960564, AW177511, AA514186, AW178893, AW949630, AW960504, AV699746, AW375406, AV700229, AV699682, AW973465, AW960474, D80248, AV718530, AV703542, AV701004, D80522, AW975623, T03269, AV720654, AV699669, AW960570, AW360811, AW179328, AW964541, AW973473, AW973445, AV720220, C75259, AV720616, AW966332, D80251, AV719000, C14014, AW352117, D80133, AW960514, AW966399, AW966333, AW966331, AW753041, AV718908, D58253, AV742001, AV742667, AV742022, AL136136.7, AF058696.1, AB028859.1, X67155.2, AF271371.1, D34614.1.

HPEBE79	456	519003	1 - 583	15 - 597	D88547.1, AB002449.1, D50010.1, AB038216.1, U79457.1, AA578773, BF858286, BF373619, BF373581, BF858371, BF373406, AV727418, AW975618, AV720791, AW964468, AV724520, AW966389, AA809122, AL535686, AV702035, AW964541, AV718692, C14331, AW966330, AV718489, AW949645, C14344, AV705869, C14407, AW973541, AV699927, AW960473, AV704548, AW964477, AW960553, AW973445, AV720104, AW949500, AV718681, D80269, AW966534, AW978648, D50979, D80227, D81026, AW966343, AV726609, AW966062, AV719758, AW962395, D59467, AV719188, AS57751, AV719632, D80195, AV718487, AV706147, AW966380, AW959062, AW964532, AW966399, AW960520, AW975605, AW966053, AW949641, D80164, C06015, C15076, AV719913, AW960465, AV654329, D59551, N66429, AW949646, AW966022, D80258, D80038, AW952852, AV720203, AW966333, AW964756, AW966050, AW966013, AW965185, AW965197, AW966041, AW965175, AV718931, AV720731, AA305578, AW975621, AV700229, AW956434, AW949658, D59503, D59275, D80045, AV720533, AW966054, H67854, AV719783, D59502, AW959597, AW959570, AV719468, AV718800, AW966400, AV720464, AW966332, AV720150, AV655880, D80302, AW949634, AW949654, AW949586, C03092, AW960483, AV723097, AW966369, C14389, AV726330, D45273, D59610, AV699866, AW975613, AW973490, F13647, AA514188, D51799, AV719644, AW975623, AW960534, AW966029, AW966075, H67866, AW966065, AW966342, D80439, AW973334, AW966531, AW978634, D58246, D81030, AV722801, AW966385, D80251, D57483, T11417, D58283, D59317, AV726423, D80157, AV720088, AW959799, AW966059, AV718938, AV694084, AV689813, AW966043, AV718633, AW959628, D50995, D59859, AW966378, AW959469, AW973485, D80022, D80014, D80166, AW973474, D80378, D80212, D80268, AW973473, D80366, AW959582, AV727414, D59889, C14973, AW965176, D80196, D80188, D51423, D59619, D80133, D80247, C14227, AV702365, D51022, AW966388, AW978661, D80210, AW965163, D80391, AV720151, D80240, D80253, AV701839, AW966030, AV719822, D80219, AV719945, AV719391, AW973307, D80043, D59787, AW973447, AV719324, AV718440, AV720028, AW952839, D80064, AW965177, AA305409, AW950578, AW965196, AV718707, AW965184, AW973488, AW966386, AW960454, AV720211, AV720291, AV720878, AW966368, AV718844, AV719557, AV720616, AV718770, AV720729, AW966032, AW973330, AW966331, AW973482, AW966398, AV699447, AW966397, AV692290, AW960532, AV700357, AW950117, AW958992, AW960514, AW958993, AW949498, AV723927, AW965158, AW959136, AV699715, AF103907.1, AF103908.1, AL359314.14, AB002449.1, AB028859.1, AF058696.1, BF976224, AV729127, AA837404, AV729103, BG055177, AW169122, AT96276, AA603456, AV729600, BF447152, BF059491, AW196971, AL566470, AL636657, AA279066, AA845528, BE219765, AV725215, AV725488, AA046476, AL025283, BF663369, BE379318, AA936074, AA031332, BF003040, BE467269, BE270829, BG060181, AA568448, AV727986, BE271012, AL351514, AW470751, AA878870, AA026888, BE879122, AA015966, AA632383, AL090910, H20001, AA150301, AV725538, AW236006, AA625391, AV704013, BE737339, AL358381, AL476276,
HPFCL43	457	535710	1 - 651	15 - 665	

HPFDG48	458	542227	1 - 709	15 - 723	<p>AI718051, AV728067, BE561457, AL048514, BF105823, AV756946, AV758524, BF576620, AA455061, AW955472, AI337508, AA026657, AI468881, AI559878, AA090696, AA455761, BF132919, BF790637, AW062362, AW149768, AA743298, AA47922, AA031331, BE839021, BG104864, AA446847, AA148792, AV702908, AV712537, AI370062, BC007349.1, AF151895.1, AF110777.1, AC007241.3, AC007742.4.</p> <p>AI005650, AW193649, T86155, R91705, R94928, T86262, R92142, T78635, BG059124, BG059311, T79120, BG105372, BE903730, F32795, AI086235, AI304866, AI094698, AI268640, AA894578, AI081163, BE856894, AI380568, R12395, BG031198, AI708047, AI358636, AI142089, AI216820, AI684336, AA804193, AA552494, AA687862, AA507473, AA879115, AA279014, AA513429, AI571415, AA918417, AI971055, AI051704, AI937021, AA099438, AI494389, AI493513, AA948053, AA581118, AI184757, AA100071, BE731794, AI879919, AI085722, AI536966, AI591039, BF124917, AI830888, AI334931, AW008928, BE274775, BE902881, BF125296, AA595467, BE281210, R71239, BE392986, BE268783, R96465, F37009, BF818912, AA401736, AA857524, AA654076, AI620153, F21367, AA292902, AF004164, AA316678, BF845471, BE694933, BF433106, AW166722, AI866691, AI859464, BE047798, AI521799, AI589947, AA713511, AW082623, AA713851, BG110241, AI918554, AW151979, AW006947, AI889379, AI049669, AV750565, BF791871, AL042191, AI345415, AA580663, AI690813, AW194014, BG029058, BF814360, AI690948, AI554343, AI866465, AI623941, AI560227, AI801325, BE965064, AW083804, AI623648, AW263569, BE393551, AI499986, AW055252, AW263804, AI627714, AI688854, AA761557, BE883591, W48671, AI287476, AI886355, AI500523, AW088605, AI433611, AW025279, BF925370, AI241763, AI491710, AI468873, AI859644, AI658566, BE879772, AI860027, AI023513, AI865942, AI648699, AI285439, AI334893, AI699020, AV757875, AW163834, AA479803, BF339548, AA999906, AI919600, BF753037, AI471429, AI539545, BE536058, AI636507, AI582932, AI305157, AI632036, N99092, R20540, AI475270, AW151132, AW827211, BE964497, AA853033, AW169784, AI440422, AI680504, AI445505, AW021373, BE875959, AA514684, BG168185, AA693444, AI584118, AA776730, AI872472, AI872489, AI887381, AA827630, AV721917, AV732941, AA761608, AI784214, AI310332, AI313032, AI696714, AI818565, AL079447, AI949510, AI653402, BF812963, AI819016, BG001293, AW020381, BG257721, BE790023, AW084233, AI868931, AI871660, AI687689, AI559596, BE541445, AW132115, AA604875, F26535, W45039, AW003866, AI500061, AI590043, AI688848, AI624293, AW020710, AI863002, AW020932, BE909551, BF673434, AW195253, AI491904, N75779, AI572717, AI524654, AI309306, AW166638, AI310575, R66759, AA449768, AW081343, BG171779, AA830396, BE962830, AI869377, AI559752, AI310582, AL042753, AW020693, AI355779, AI581033, AI340533, BE887861, AL037602, AI263584, AW168708, AI819976, AI669640, AI818980, AI621341, AI868204, AI597748, AI499325, BF909758, BF337602, AL009172.1, AB016194.1, BC000720.1, BC008890.1, AF092737.1, AJ012755.1, AC069298.8, AK027188.1, BC008364.1, AB063084.1, AL136889.1, AC004213.1, BC009026.1, BC001675.1, BC002688.1, AK000501.1, AL137705.1, AB050533.1, AL389951.1, AL050393.1, BC001963.1, AL389935.1, AK026865.1, AB050410.1, AL133623.1,</p>
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HP/AQ68	459	833082	1 - 2452	15 - 2466	<p>AK000489.1, BC002481.1, BC007241.1, BC003682.1, BC002523.1, AF217982.1, BC008840.1, U51587.1, AL136748.1, AL499604.9, BC005402.1, BC008078.1, AL080126.1, AF061573.2, AL133325.20, BC004960.1, BC001294.1, AL137478.1, AK025435.1, AB048954.1, BC002733.1, Z94277.1, AC005291.1, U66059.1, D83989.1, U95739.1, AF168787.1, AL137463.1, AB050534.1, BC006345.1, BC002574.1, AC008014.5, AL353802.14, BC006480.1, S76508.1, AL133665.1, AP001434.1, AC005353.1, AP000020.2, AP000161.1, AC012502.3, AL022147.3, AC005048.2, AC005968.1, AL157360.8, AL162713.19, AC025754.4, AL391873.15, AC006222.1, AL359997.8, AC009144.5, AC007056.4, AC008592.4, AP001731.1, BC003683.1, BC009395.1, AB063074.1, AL136915.1, AK024747.1, S77771.1, BC008673.1, BC007417.1, AL133070.1, AK026590.1, AF217987.1, BC002524.1, AK027204.1, AL512718.1, AF369701.1, AL137292.1, AL137658.1, BC000860.1, BC003056.1, AF091084.1, AL117438.1, AF038847.1, AL117587.1, AK027103.1, BC007456.1, AL117460.1, AB055303.1, AB060887.1, AL023657.1, AK000647.1, AC007597.3, BC003637.1, BC006251.1, AK026642.1, BC002355.1, AF141289.1, L30117.1, AK000247.1, AK024855.1, AL136765.1, AL137547.1, AL080137.1, BC008417.1, AC010972.3, AL121932.19, BC004943.1, AK026649.1, AK027111.1, AK026542.1, X82434.1, BC002365.1, AK027102.1, AF358829.1, AF073483.1, BC002541.1, BC006196.1, AL080139.1, BC004310.1, BC006458.1, AF124728.1, AK025254.1, AF321617.1, AK026551.1, AK024545.1, BC002476.1, AL161427.16, AL137537.1, AF110329.1, BC003052.1, AB048913.1, BC008429.1, BC002914.1, AK026164.1, AL133640.1, BC002970.1, AK025798.1, AB060869.1, BC003548.1, AK027614.1, BC008751.1, AL137548.1, AL355795.13, AC010088.3, D55641.1, BC006119.1, AB050407.1, BC002752.1, BC002519.1, AB060877.1, BC004222.1, AK025414.1, BC003569.1, BC002631.1, BC002448.1, AB055368.1, BC006093.1, AL353940.1, AF002672.1, AL354828.12, AC019176.4, AL049276.1, AK026593.1, AF026816.2, AB050411.1, AL390154.1, AK000137.1, AF054988.1, AB049900.1, BC008488.1, AK027173.1, AL389957.1, AL137538.1, AB047869.1, AB060888.1, AL136893.1, AF125948.1, AB063087.1, AL096728.1, BC006161.1, BC001844.1, AK027136.1, AL137479.1, AL110280.1, AL137267.1, U67211.1, AL390167.1, AF334536.1, BC003687.1, BC003587.1, D44497.1, BC003110.1, AK026793.1, AB060861.1, AB048921.1, AL390079.1, AB060903.1, AK025391.1, BC001217.1, AL359600.1, AB047609.1, BC003602.1, AJ012582.1, AL512719.1, AF179633.1, AK026857.1, AC003032.1, AC025735.4, AC023880.5, AL096776.12, AL034374.2, AC010137.3, AC007719.7, AL109800.25, AL360297.12, AL022170.1, AC006338.5, AC021020.3, AC026888.6, Y14040.1, AF261134.1, AK024524.1, AK000753.1, AK000450.1, AF042090.1, AJ001838.1, U92992.1.</p> <p>W89022, W89021, AA400091, AA480871, AA480928, AA400180, H72944, H72544, AV731860, N62805, AI827122, AF742541, AI820089, AI650350, AI499934, T17487, AI922817, AI590848, AI679031, BE141338, AV720191, M85961, BE093537, AW893527, AW893524, AA909164, BE093538, BF222081, AL049831.2, AL138776.10, AC004825.2, AC005539.1, AC008151.1, AC006152.3, AC008085.1, AL139141.22, AL133512.10, AC073310.7, AC002069.1, AP003547.2.</p>
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HP1B015	460	131086 8	1 - 1725	15 - 1739	AL353133.7, AC011716.7, AC004070.1, AL391559.13, AC011286.7, AL133238.3, AC026116.26, AC002068.1, AC007463.3, AC007632.4, AC080011.21, AL035409.15, AL096888.30, AL136130.7, AL391557.11, AL512272.15, AL109913.20, AC002402.1, AC009302.2, AL356750.16, AC006324.3, AL133342.14, AL590635.7, AL160008.3, AC007253.2, AL035070.3, AC025577.15, AL035451.5, AC016902.4, AL445240.8, AP000802.4, AC012152.12, AC009757.8, AC016648.5, AC026441.4, AC000122.1, AC024028.10, AL139112.9, AC019197.7, AC010738.4, AC015933.8, AC007631.3, AC010351.6, AL034409.4, AC012081.16, AC024603.5, AL079352.3, AL442166.1, AL137861.5, AL163284.2, AC008170.2, AL008729.1, AC040171.3, AC006034.2, AL355537.11, AC009496.3, AL445225.9, AL365400.19, AL022154.1, AF001552.1, AC007639.5, AC005083.1, AC006925.6, AI056404, AI802391, AW270724, AI750249, N41425, N47678, AI188511, AI376981, AA029314, AW452123, BE466507, N39755, AI937190, AA063620, AA693737, AI139466, AA701241, AI250789, AI672263, AI198257, BF055537, AI199035, AA677064, W69895, AA040154, BF196981, W73711, AA029867, W69841, BF222273, AW900121, AW022270, W69574, AI373227, AI200161, AA701858, AV690112, AW044223, W69662, AI052153, AA872860, H29417, H29324, N26312, AI283749, AA036704, AI383659, AA332627, N47677, AI424682, BE089934, AA329748, AW952484.
HP1CB53	461	104230 9	1 - 1125	15 - 1139	AI284640, AL079734, AI345695, AA410788, AI128592, AV760508, AA449997, AU147162, AV756491, AW302315, AI801482, AW265385, AW021583, AW265393, AI733856, AA521323, AW963117, AW327624, AV763026, AV763058, BE150796, BG059568, AV759204, AV760915, BF827410, BE147833, BE062478, AW969941, AW062724, AA634786, BE063437, AA521399, AV764259, AV763971, AW270258, AI491765, AA666332, AW302909, AW504485, AW974932, AI908093, AI753488, BG236735, AW963463, BF681619, AA581903, BE139267, AL120343, BF804385, BE062476, AI669589, AW402458, AW189068, BG236628, AV759632, AA584489, BF989483, AI610468, AI244127, AW467323, AW271904, AW630298, BE872393, AV759274, AW805539, BE393367, AW189113, BE139358, AW970877, AI732483, AI754037, AW845366, AA468022, AI251576, BF030641, AV761519, AA643770, AW237905, AA284247, AW084445, AW148507, AW439558, AI612142, AI358384, AI471691, AU118374, AL040034, BF750422, BF761328, AW020992, AA469327, AU147922, AA469451, AA704393, AL037910, BF736198, AW503900, AV758903, AV703785, AL038936, BF949490, AL048616, AA483256, AW021917, AV762395, AW062682, BF965775, AV713243, AA916430, AA857296, BG029528, BG009317, AI708009, AV762982, AW268232, AI306232, AA661948, AV744179, BE062545, AA515048, AI583466, D83989.1, AF077058.1, X75335.1, X55926.1, X55931.1, AC018690.5, U18398.1, AP001208.3, AC005399.19, AL096755.1, AC018494.6, U02531.1, AP001330.3, AI003147.1, AL121586.31, AL137792.11, AP000251.1, AC018511.4, AL356915.19, AL133347.28, AF091512.1, AL160163.24, AC002316.1, AL022336.1, AP000212.1, AC011471.6, AC018695.6, AP001711.1, AC006487.8, AP000030.1, AP000134.1, AC005037.2, AF288742.1, AC005342.1, AL050318.13, X76070.1, AC011462.4, AC004126.1, AC006435.7, AC074331.1, AC005089.2, AL162718.15, AC072052.6, Z96568.1, AC007272.3, AL033529.25, AL163636.6, AC009228.4, AC005520.2,

	462	101146 7	1 - 2634	15 - 2648	AP001760.1, AC006333.3, AL096817.12, AC005519.3, AC005215.1, AP000557.2, AC005207.1, AC005102.1, AC005088.2, AC006077.1, AC004531.1, AL353140.12, AC009068.10, AC087225.1, AC004841.2, AC004583.1, AC009131.6, AC002996.1, AC002301.1, AL022323.7, AP205588.1, AC007957.36, AL449212.1, AC019206.4, AC010913.9, AL109797.18, AL078621.19, AL034417.14, M87898.1, AF317635.1, AL157823.9, AP001759.1, AL031658.11, AC002036.1, AL035555.10, AC068319.4, Z93023.1, AC007383.4, AL136979.16, AP000501.1, AL138499.4, AC000073.1, AC024576.5, AP001753.1, AC010422.7, AB001523.1, AP001717.1, Z85987.13, AC005593.1, AC006509.15, AL122004.17, U73023.1, AL031681.16, AL157372.18, AL158830.17, AC007308.13, AL139378.15, AC026185.3, AC007546.5, AC005740.1, AL138692.26, AC007421.12, AC006992.2, AL356532.9, AL137784.14, AL034420.16, AL445664.14, AC005522.2, AP000556.2, AC010363.6, AC007707.13, AC006511.5, AC023490.5, AC004821.3, AC011472.7, AC018633.2, AC005531.1, AL133448.4, AC004103.1, AP000115.1, Z82182.2, AC012450.9, AP002810.3, AL161454.10, AC010458.5, AC009756.9, AL031596.7, AL136984.20, AC009309.4, AC026439.3, AL159970.16, AP003357.2, AL121826.11, AL035450.1, AJ009610.1, AL139353.3, AL050404.3, AC090942.1, M63796.1, AL356796.16, Z84469.1, AL033528.19, AC079175.24, AC004826.3, AC004921.1, AC026161.4, AC083871.2, U91323.1, AC000085.5, AC004824.3, AC022415.5, Z84486.1, AC006130.1, AL590031.6, AL109952.15, AL136452.7, AL353748.13, AC009086.5, AC006195.1, AP001101.2, AC004967.3, AC023869.5, AC018808.4, AP001060.1, AL158823.11, AC006483.3, U47924.1, AL132772.14, AF196969.1, AL590762.1, AC010150.3, AL136303.15, AL391595.14, AC073193.10, AC008946.6, AL031291.3, AC005387.1, AL136992.22, AL136172.16, AF312032.1, AC009087.4, AL355392.7, AC024028.10, AC005057.2, AC005231.2, AC002350.1, AC034198.6, AC022201.4, AC067722.21, U29895.1, AF053356.1, AC024166.3, AF336797.2, AC007637.9, AP000306.1, AL445532.8, AC025280.4, AC004662.1, AL021939. 1.
HPJBK12	462	101146 7	1 - 2634	15 - 2648	AP001206.3, AP001329. 3.
HPJCL22	463	114667 4	1 - 3093	15 - 3107	AU140137, AW273142, BF511622, AW500031, AW997852, AW997845, AW997846, BE263631, AW997843, AI457507, AW449421, AW451219, BE047152, BF946370, BF439925, BF946380, AI200349, BF897509, BF512501, Z19075, BE827516, BF094042, BF094020, BE244735, AA325330, AW962065, R31240, AI023715, AA736958, BF802328, BF988285, BG015997, AA215423, BF736763, AW997844, AA285156, AI254765, BF902055, BF724699, AV740801, AA847952, AA634889, AI284640, AA074818, AL134972, BF724366, AW274349, AV763138, AA468131, BF946053, BF945647, AV729809, AW303196, AI801148, AL038072, AA873777, AL133662.1, AB020720.1, AB051126.1, AK023742.1, AC020916.7, AL512802.2, AC005098.2, AL109758.2, AK024937.1, AL096701.14, Y11535.1, AL080243.21, AL137073.13, AL137059.20, AL590709.5, AP002378.3, AL158210.12, AC006064.9, AC002563.1, AP001064.1, AC017016.5, AC004836.2, AF238380.1, AL021918.1, AC018641.3, AL136162.17, AL035460.15, AC084356.22, AC005943.1, AL157877.11, AP000760.4, AC021752.5, AC011446.6, AL121895.26, AL451075.15, AC011308.8, U67829.1.

HPICW04	464	589969	1 - 1452	15 - 1466	AL034429.1, AL049776.3, AC003043.1, AF059321.1, AP001748.1, AC074115.4, AL133622.1, AC016138.8, AF052144.1, AL136295.3, AC005007.1, AC018618.5, AC026672.44, AC016597.4, AL136305.14, AL352979.4, AL133545.10, AL360169.17, AL031587.3, AC026184.3, AC074121.16, AC044797.5, AL117382.28, AL358293.4, AC007546.5, Z95152.1, AK022069.1, AC010618.7, AC011470.5, AL157912.5, AL022721.1, AC004084.1, AL157789.6, AL137495.1, AC005015.2, U07562.1, AC073492.18, AC005144.1, AC008635.6, AL035704.9, AC067722.21, AL121829.30, AE006464.1, AL590763.1, AL049610.9, AL137244.28, AL162272.10, AF754983.2, AP002371.3, AC010527.5, U73023.1, AC020904.6, U91322.1, AC012306.11, AL352984.4, AC020955.6, AC018523.9, AC004928.2, AF015156.1, U95739.1, AC027319.5, AL138717.6, AL163201.2, AC008555.5, AC011497.6, AC019206.4, AC007005.3, AC018504.4, AC020552.4, AC068313.4, AC004867.5, AL355392.7, AL021397.1, AC010312.4, Z97630. 11.
HPICW04	464	589969	1 - 1452	15 - 1466	T81065, H59556, T70276, H59557, AC002519.1, AL136123.19, AC090051.8, AL021579.1, AC010202.6, AC025589.20, AC022267.8, AL359272.9, AC022148.5, AC009756.9, AC078962.30, AL356121.13, AC007880.2, AL137793.16, AC002059.3, AC008450.5, AC010654.8, AP003114.1, AC007226.3, AL033519. 42.
HPJEX20	465	135242 0	1 - 552	15 - 566	AW938132.
HPMAI22	466	635491	1 - 1260	15 - 1274	AL540210, AW173208, AW006589, AV707182, AW104434, BE503183, AL148598, AL656207, AL350808, BE035507, AW297121, AW237250, AA918535, BF057772, AA918200, AL357673, AW235193, AW083055, BE053001, AL350807, AL200477, AI991567, AA953496, AL825590, AA738163, AW962712, N59298, AA369466, H71562, AA369367, AA369366, H71045, T48746, H71557, AL354716. 9.
HPMFP40	467	638165	1 - 1203	15 - 1217	U48436.1, AC005731. 2.
HPMGJ45	468	798102	1 - 1642	15 - 1656	AI800816, T70609, AA001037, T70876, AW295609, AI174704, AA488148, BE818897.
HPQAC69	469	396804	1 - 976	15 - 990	BE825496, Z21226, AL159154.16, AF075587. 1.
HPRBC80	470	829136	1 - 2529	15 - 2543	BF508706, BG251902, BG118348, AL522364, AL690187, AW959485, AV705315, BF672789, AL520227, BG176557, AL528876, AV713609, BE439925, BF130665, AW963928, BF994344, AL536566, AA446397, AA180531, BG026529, AA180520, BF672895, BF029282, BF670440, BF799935, BF510400, AA179618, AL513906, BE246173, AA625572, BE244085, BF671786, AI681635, BE004437, AA431963, AV701964, BE566300, AV653358, BE004444, BF790083, Z30124, AI164383, C17250, AA379401, N24451, AA363823, BE004648, AA180509, AV713647, T35331, AW961450, BF800059, AV686722, BF575322, AW020971, BF229438, AW361378, AA465249, AA313690, BF979498, BE694196, AW999825, T35345, AA625571, BE925937, T30431, AA135096, BE172414, BF980120, N54675, AW897938, BF210564, AW665936, AA769851, Z20951, AW242738, Z19798, C16481, AW197150, AL567621, BE222028, BE622950, AW883664, AA885770, AI039327, AA628005, N50019, AI650889, AJ271835.1, AF136972.1, AC013717.8, AJ271832.1, AF294792.1, AI005801. 1.

HPRBF19	471	753282	I - 1447	15 - 1461	AW582253, AW469181, A1799626, BF375244, AW469177, A1921465, AU157797, A1697014, A1346622, AW029127, C05837, A1830044, A1285194, A172076, A1281230, A1285227, AW452356, A1278830, BF508192, A1283827, A172244, BF375243, A1612697, BF378919, AW589436, BE183571, AW365013, A1264367, C00562, AW869793, BE002927, A1473464, A1925050, A1362363, A1270207, AA371314, AU138880, AW814058, A1476009, AA314891, AW008169, A1571538, BE814188, AK023655.1, U91321.1, AC003108. 1.
HPTTG19	472	635033	I - 545	15 - 559	AA968657, AA493322, AW964196, AW945159, AW950095, AW963925, AW949384, AW951182, AW952751, AW949383, AW962651, AW963933, AW964422, AW958763, AW956474, AW960718, AW964284, AW967195, AW960207, AW954032, AW957083, AW959366, AW949682, AW962713, AW958568, AW958569, AW949767, AW951201, AW963026, AW949757, AW957085, AW949750, AW953772, AW954070, AW960237, AW957062, AW949697, AW967372, AW955902, AW958365, AW950217, AW954506, AW966270, AW964223, AW958756, AW955977, AW955982, AW951187, AW949856, AW951437, AW953773, AW962636, AW952126, AW957059, AW964421, AW954068, AW949551, AW949863, AW962650, AW950219, AW961026, AW963025, AW964203, AW949552, AW957068, AW958225, AW960720, AW951452, AW966421, AW962648, AW964012, AW958740, AW959899, AW955892, AW959356, AW949761, AW949762, AW964198, AW951430, AW963027, AW964420, AW963915, AW953657, AW955900, AW945197, AW965978, AW956278, AW951409, AW952743, AW951624, AW951197, AW949764, AW957061, AW964224, AW949850, AW962649, AW962644, AW964423, AW953769, AW965895, AW949759, AW963931, AW963940, AV706741, AW953807, AW945155, AV707067, AV707786, AV702794, AV705836, AW961247, AV707234, AV727499, AW955724, AW965899, AW956626, AW965869, AV704974, AW965866, AW957677, AW961052, AV702716, AV725181, AW951184, AV709772, AV705660, AW965033, AW963011, AV703239, AV702990, AV661286, AW950678, AW963962, AW961400, AW963598, AV704490, AW959270, AW956792, AW952418, AW950240, AW966389, D50992, AV705590, AV704497, AV706871, AV704891, AW963631, AV688823, AV701911, AV693604, AV705273, AV695888, AV727353, AV707576, AV703275, AW964074, AV705282, AW967052, AW951738, AV703453, AV707368, AW954228, AV709635, AV687035, AV708304, AV701769, AW961255, AW960629, AV702964, AV707331, AV707197, AW949517, AV703742, AV705710, AV701667, AV726551, AV652860, AW953804, AW957674, AV709248, AW951768, AV728539, AW953797, AV728953, AV649758, AW954697, AW963405, AV704785, AV705453, AV708872, AV727314, AV654686, AW963087, AV706876, AV703457, AV706453, AV709527, AW950520, AV701730, AV705909, AV728282, AV707059, AV702637, AV703591, AV704124, AV702306, AW962983, AV705757, AW951773, AW959804, AV728999, AV709596, AW950671, AV729532, AV708610, AW963700, AV706579, AV707909, AW950006, AV707238, AV709725, AW964490, AV706910, AV729198, AW961313, AW956618, AW956619, AW956624, AW958455, AW955710, AW964429, AW950778, AV726337, AV703553, AV704376, AV656478, AW959846, AW958161, AW952328, U73636.1, U94592.1, Z30183.1, U45328.1, AB005666.1, Z79435. 1.

HPVAB94	474	526749	1 - 805	15 - 819	AI862453, AI590769, BE301273, AI569794, AI800423, AI859970, BF982756, AI653897, AW170296, AI811162, AW467390, AI653548, AI653548, AI739622, AI739622, AW276481, AW473524, AI963681, AI701477, AI657090, AA973284, AI624062, AA884426, AW007927, AI671878, AW300934, AI150198, AI597690, AA687348, AW964953, AW772043, AW205152, AA398522, HI6789, AA639818, BE856046, T72002, BE939495, AW518068, AW079395, AW510732, AI283535, AI028345, AI208208, AA847299, AW025171, AI204112, AI869844, AW235822, BE313614, AI521850, R48787, AI917108, T87641, BG236404, AI760407, F09217, AA835697, AW009374, AI200294, AW136297, AW578241, AA609623, T51196, AA132853, AI222636, T03597, T80196, AA046518, BG181058, AI648526, AA046693, AW196234, T51302, AI297158, BF591885, AI784267, BF222991, AI656095, AI539547, AI673418, T64280, AA160800, R50052, BE892957, AA927052, AW194685, AI283529, AW274852, AA292781, AA298687, AI247295, BE386015, BF348744, BC009302.1, AK026044.1, AF288687.1, AB038728.1, AF060515.1.
HPVAB94	474	526749	1 - 805	15 - 819	BF370024, AW449056, AF131217.3, AI163247.2, AF165147.1.
HPWAY46	475	100156 0	1 - 1400	15 - 1414	AW857326, AW861371, AV661974, AW857769, AW861551, AV661986, AW937024, BF130874, BE067001, AW861563, AA460256, AA908484, AI804404, AA235344, AI827237, AW833214, AI682922, AI306704, BF382808, AW151460, AW294348, AA336017, AI553689, BE066930, BF914075, AI016721, BF507352, BF114874.
HPWDJ42	476	722246	1 - 1326	15 - 1340	AA651639, BF668217, AL046409, BF677892, AA581903, AW518220, AW303196, AW301350, AW274349, AL119691, AW964231, AW327624, AI696955, BE160727, BG059568, AA521323, BF130605, H05940, BE910362, BF769368, AW979060, AI281881, AW858127, AA521399, AA148672, AW965008, AL042853, AV734666, AV762033, AA167055, AV761519, AW513362, BF965007, AW975012, BF724699, AW270382, AC018738.4, AC006262.1, Z69714.1, AL109952.15, AL109897.30, AC008760.6, AC005939.1, AC004687.1, AL158040.13, AC011737.10, AC008745.6, AL050321.11, AL034420.16, AC004854.2, AC007216.2, AI400877.1, AC004150.8, AL117692.5, AC004033.3, AC068799.14, AF015151.1, AF015156.1, AC007731.14, AC080012.20, AC010422.7, AL358354.16, AC053467.1, AL118502.38, AL121969.12, AL035079.14, AC005921.3, AC005209.1, AC005098.2, Z95115.1, AL121989.12, AL354720.14, AL033529.25, AC004417.1, AC010328.4, AE006639.1, AC004166.12, AC008750.7, AL049761.11, AL096701.14, Z99716.4, AL139317.5, AL024509.1, AC002418.1, AC005500.2, AC018809.4, AL133245.2, U95742.1, AC010203.13, AC008626.5, AL022316.2, AC007030.3, AC004386.1, AL353748.13, AL022329.9, AL121928.13, AL139353.3, AC012368.6, AL591398.2, AL355334.26, AC004821.3, AC004590.1, AL135901.23, AC084864.2, AC023160.31, AL359402.3, AP000212.1, AP000134.1, AL109984.14, AC007510.6, AL359235.3, AC006480.3, AF312032.1, AC009086.5, AC022308.17, AC009298.3, AP003357.2, AL359846.11, AL390074.17, AC005368.1, AC011895.4, AC005040.2, AC007963.7, AP002851.2, AL365225.12, AC022383.3, AC022596.9, AC023892.35, AL137784.14, AL359541.11, AC006948.4, AC005252.1, AF279660.2, AC010319.7, AL021807.2, AC007620.30, AL109933.25, AL078477.5, AF348209.1, AC009961.11, AC009996.7, AC006511.5, AL136137.15, AP001729.1, Z98036.1.

					AC006345.4, AP001671.1, AL355096.4, AL355512.22, AC006483.3, AP001700.1, AL109825.23, U96629.1, AC009228.4, AL138976.5, AL136980.5, AB043547.1, AL359091.10, AC010530.7, AC004771.1, AC007308.13, AL157369.7, AC011452.6, AC005037.2, AC005666.1, AL138807.12, AC008882.6, AC006435.7, AC022148.5, AL133453.3, AC012072.2, AC007488.15, AC002045.1, AC005553.1, AC003982.1, AL022476.2, AL121655.1, AP001038.2, AC017067.4, AL137141.10, AC002351.1, AL109743.4, AC009244.24, AC005821.1, AC004253.1, AC069277.5, AC007383.4, AC021752.5, AL034555.2, AC006571.12, AP001711.1, AC004955.2, AC006509.15, AC026179.5, AL122035.6, AF190464.1, AL023494.12, AL356515.17, AP000553.1, AC022211.5, AC026368.37, AC012309.7, AC004477.1, AL135818.3, AC011900.6, AF030453.1, AC069475.27, AC024154.2, AL139100.9, AC019060.5, Z98941.1, Z85986.1, AL049636.22, AL135927.14, AC007227.3, AF244812.1, AP000306.1, AP000246.1, AL136301.21, AC087590.1, AP001619.1, AC005971.5, AL049709.18, L44140.1, AL355916.2, AC010583.5, AL138692.26, AJ295844.1, AC011500.7, AC011515.4.
HPZAB47	477	585702	1 - 1662	15 - 1676	AW993896, AA493291, AA526359, AW972615, AL720194, AA358397, AW204400, AA508549,
HRAAB15	478	658717	1 - 1733	15 - 1747	BG111918, A1823987, A1807761, AW165961, A1418806, A1738753, C05983, BG152897, A1439250, BF327504, AA923586, A1424510, BE003132, BF894183.
HRABA80	479	882176	1 - 1237	15 - 1251	AU147250, F24079, A1791459, A1732503, AA523577, A1791342, AU121439, BF309840, BF308519, A1659402, AA719317, AA602233, A1752815, AW967109, AV694013, AA470486, A1218622, AA644545, AK022184.1, AC005777.1, AL031431.8, AC007406.1, AC032011.14, AC004143.1, AC006131.1, AC074121.16, AC005760.1, AC005529.7, AL354766.17, AC025166.7, AC012476.8, AC005544.1, AL035079.14, AL356299.16, AL031297.4, AC005778.1, AC011666.28.
HRACD15	480	871221	1 - 1525	15 - 1539	AL519765, AL519766, BE910445, BF684654, BE270497, BE513843, BF975936, BE396890, BF973472, BE515166, BF686665, BE744708, BG257119, BE880162, BE797305, AW248552, BE514176, BE793786, BE791776, BE296702, BE271500, BE268991, AW512838, BE791090, BE727326, BF026627, BE797018, BE275277, BE277906, AU133849, AW248687, AU120611, BE270509, BF027092, BE384166, A1563668, BE513807, AW405789, AU151587, AA261853, AW043669, BE729554, A1949119, AW575486, AW751019, A1524253, BE391940, AW245114, AU145208, BE312276, BE796133, BE561087, A1953094, BE390017, AA283855, BE265439, BE391036, BE391843, A1620547, AW402545, A1075157, A1744741, BF125945, BF941740, W60104, BE266246, AW085553, AW131075, A1768378, AA401964, BE390215, A1752668, BE736619, AW967867, A1565659, BE387591, BE222775, AA283856, AW750999, AA261854, A1498229, AA830894, W60024, AA496293, A1660481, BE960924, BE277521, AA994223, AA868400, BF026241, BE382766, A1801124, BE671092, A1264882, A1355420, AW248994, BE503489, A1262893, AA583344, BE266582, A1832018, N29665, AA622755, A1439625, A1193362, BF446254, BE504260, BE387503, AW806699, AU146635, BE856089, A1087826, BF801189, AA133817, AA843858, A1287716, AA928793, AA699788, A1027345, BE728607, AW629986, W52804, T10369, AW103963, AA933691, BE138812, A1284845, AW264928, AW152071, A1265798, A1809041, A1038469, AW246086,

HRACD80	481	130977 4	1 - 1927	15 - 1941	AI435409, AV691151, AW957437, AI620834, AI452870, AI860541, AI475835, AI418409, AI744163, AW002187, AV692842, AI521647, AA845397, AI744800, AW002140, AI309558, AU118709, W96176, AW768771, BE207457, AW236670, AW264115, D29066, AO026580, AA135589, H55790, AW732194, BG006063, AI024919, AA256768, AI214884, AA280734, AA565467, R87509, BF056311, AA643222, AI024305, BF204467, AA077296, BF310268, W07856, T30234, R48997, AI435115, AI567828, AI537884, AW050631, AI740587, BE162565, BE149783, AW090152, T10368, AW627586, AI537596, AA622914, T50404, AW016161, W45022, AI274609, AA570075, AL039562, AA827726, AW246353, W04715, H89133, BF125722, AA626654, AW246566, AW519242, AI659744, AI752669, AW247535, AA077415, AW129363, AI202252, AA628809, BE869982, AI208476, BE206952, AW511835, AA037397, BF828156, BG031018, BE513491, BE736901, AW149144, AI189756, AA078651, BE513973, BF194732, H47888, AW954928, AA806404, AW080710, BF847605, AA077110, AA319080, AA101354, AI214676, AA434187, AA932091, BF837875, BE140453, AA428843, R11194, AA778244, AA077601, AW082443, N90686, AI675644, BF794477, W05073, AI520907, AL046053, AW298462, AA496322, T50535, BC008084.1, AK001129.1, AK021688.1, BC007488.1, AL117583.1, AC006014.2, AB014518.1, AC005488.2, Y16704.1, N54250, N81046, AA036807, AA135546, AA236044, AA262692, AA938381, AA204918, AA402082, AA455506, AA455507, AI217271.
HRACD80	481	130977 4	1 - 1927	15 - 1941	BF001770, AI431600, AI332903, AW778829, BF197765, AI814110, BF875981, BF509841, AI983390, AI741104, AI263763, AA719400.
HRDDV47	482	637650	1 - 1496	15 - 1510	BG035895, AI271436, AW510873, AW341493, AA833696, BF205827, AA280770, AW137710.
HRDFD27	483	567004	1 - 791	15 - 805	W85784, AI254961, AA767643, BG164474, AA428410, BG007947, AI625142, AI111171, AC005274.1, AC004491.1, Z68192.1, AL365225.12, AL033529.25, AC009086.5, AC008569.6, AC002420.1, AC022392.4, AC012170.6, AC008474.7, AL157912.5, AC004966.2, AC002551.1, AL035695.17, AC005184.1, AC002115.1, AC027319.5, AC020610.6, AL121777.39, AC024568.4, AC009412.6, AC009055.2, AL133453.3, AP003352.2, AL163248.2, AL118520.26, AF260011.2, AC005940.3, U95742.1, AL022396.1, AC005362.1, AC004841.2, AC007676.19, AC024578.3, AC0059762, AW015128, AW753637, AV711012, AA296493, BE151396, AV655181, AI220561, BE006108, AA311800, AW962850, AW516636, BF881635.
HROAJ03	484	567005	1 - 1168	15 - 1182	AA372458, AC004189.1, AP000517.1, AB023054.1, AC009313.4.
HRTAE58	485	519326	1 - 586	15 - 600	BG056575, N22501, AW884147, BF903801, H59173, AW963463, BF997339, AW958318, AA374525, AW502694, BF816190, AA364420, AA378207, AA810158, AC007130.2, AL122035.6, AL353692.14, AF124523.1, AL391122.9, AL035404.20, Z93241.11, AC007917.15, AL353680.8, AC005881.3, AC005740.1, AP002851.2, AL133477.16, AC004805.1, AC008891.7, AL390882.12, AL031602.14, AC005015.2, AL133479.11, AC005920.1, AL136228.8, AL139317.5, AL137792.11, Z84487.2, AF205588.1, AC007782.20, AD000092.1, AC025594.5, AL109804.41, AJ009612.5, AP000557.2, AC072061.8, AC083884.6, AC005529.7, AL133243.1, AL096791.12, AL137802.7, AL133410.31, AF243527.1, AC005399.19, AB026898.1, AC004883.2, AL392166.19, AL050318.13, AP003357.2.
HSATR82	486	531973	1 - 763	15 - 777	

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HSAUK57	487	772554	1 - 1023	15 - 1037		AL801272, AW510484, AW938669, AW963599, AW964519, AV703063, AW962942, AW967052, AW961606, AW967329, AW961841, AV727589, AW962648, AV725024, AW726532, AW963592, AW963349, AV728841, AW950748, AV728138, R47506, AW962444, AV707331, AV707907, AV687010, AW963895, AV704876, AW963486, AV702738, AV702975, AW954242, AV742541, AV702107, AW963608, AW964860, AV688658, AV708167, AV704541, AV652563, AW964213, AW957644, AV721745, AW962321, AV691793, AW962155, AV707237, AV703844, AW963652, AV702172, AW962136, AW963498, AV707135, AW961299, AC012076.4, AL049780.4, AC008736.6, AC008395.6, AP002841.2, AL160269.14, AC004166.12, U95742.1, AC007216.2, AL121972.17, BF793712, AW080832, AI693734, BE869501, AI564525, BF037343, AW475057, AA523950, AV719716, AW024144, BF827012, AI185475, AI197788, AV660309, AI708671.
HSAVH65	489	545459	1 - 586	15 - 600		AL821931, AW303196, AW301350, AA397389, AI821714, AI792133, AI791913, AI821785, AI755057, AI336054, AI357823, AV760453, AI291823, BE328573, AI369580, AI039809, AW872676, AI479148, AI559645, AV762354, AW327961, AW872575, AW079761, BF347791, AP002851.2, AF224669.1, AC012066.10, AL035420.15, AL1354707.17, AL078581.11, AF001549.1, AC007739.2, AL391839.9, AL135778.9, AC018690.5, AC005028.1, AL022238.1, AL139343.9, AC011452.6, AP001718.1, AP001671.1, AP001972.4, AC003969.1, AL049541.24, AC006011.2, AC005005.1, AP001694.1, AC005914.1, AC004913.2, AF196969.1, AC090051.8, AL133453.3, AC008511.6, AL354720.14, AL121981.17, AC005531.1, AL355499.15, AC073581.23, AC007256.5, AL096791.12, AP000553.1, AL133320.8, AC090527.3, AL160237.4, AC005859.1, AC003691.1, AL357992.14, AC023469.6, AC004554.1, AL445143.2, AC024075.4, AC005701.1, AL137072.8, AL139415.10, AC016656.5, AC016652.5, AL163248.2, AL449264.18, AC023795.18, AC006203.1, AL353135.32, AF314058.1, AC004104.1, AL136300.22, AL136358.13, AL590762.1, AL389888.8, AP000692.1, AC006946.20, AL035458.35, AL022318.2, AC005157.1, AC020728.4, AL136139.6, AC021810.7, AC005071.2, AC068724.7, Z84572.1, AL021578.4, AL450263.15, AC008840.4, AL355103.3, AP001709.1, AC005962.1, AL163281.2, AL138820.11, AC006329.5, AC005291.1, AC009481.4, AL034380.26, AL161747.5, AL117356.5, AL163282.2, AL008639.15, AC002990.1, AC008591.6, AC005519.3, AC003683.2, AP001706.1, AC008271.6, AP001670.1, AL133246.2, AC010203.13, AP000555.1, AC008945.6, AC026749.5, Z83826.12, AL139350.17, Z98050.1, AC010422.7, AL139801.17, AC011451.6, AL133355.12, AC026866.8, AP001725.1, AP001712.1, AL009182.17, AF111167.2, AL161804.4, AL022162.1, Z93023.1, Z97989.1, AC022116.5, AC005089.2, AP001667.1, AC007277.2, AP000642.5, AC013416.4, AC010543.8, AC002527.1, AL121755.23, AL034372.33, AL122021.3, AC013471.7, AC006040.3, AC006001.2, AL138706.9, AC034305.6, AL133396.2, AC006430.22, AL162464.5, AL353764.9, AP000901.5, AC006211.1, AL163218.2, AC007991.7, AB053170.1, AC022217.5, AP001705.1, AC004847.3, AL049762.20, AC004914.1, AC083855.2, AL136305.14,
HSAVK10	490	561435	1 - 1228	15 - 1242		

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HSAWD74	491	460527	1 - 956	15 - 970	BG056446, N32720, AW152171, AA339555, AA076697, AA525291, AA380007, BE734992, AA077031, AA379882, BE047929, AA515728, AL282253, AA683069, AW275432, AW274078, AA533025, AI675615, AL040054, AA644090, AI345123, N42169, AW023111, AV756491, AI962030, AV758870, AW021774, AA602906, BG222564, BG222326, AV762454, AL048060, AA225406, AI879951, AA078830, AW514006, BE063437, BF725844, AI591299, AI590522, H68343, AA825827, AA559166, AW272294, BF213224, BE049095, AI344810, AA714011, AW502237, H63660, H24331, AA171400, AL449689, AI753113, F18888, AA282951, AV761486, AW193493, AA669238, AI557644, AI049868, AW631267, AA525331, AW117740, AA507623, AA862183, BE968744, BE677164, AW571963, AI433952, BF991881, AA701080, BF970107, BF212465, AA832175, AA470933, AW157128, AI343144, AW974751, AW338376, AW410409, AW844636, AW664505, AA827383, AV760014, AI745116, AI003611, AV683406, AW021154, AW501278, BE968477, BF991882, AI189682, AU124213, AI336637, AW572140, AA610644, AW963463, AA708322, AA489390, AI887235, AC004084.1, AC004951.5, AP000252.1, AP001711.1, AC006160.9, AP000031.1, AC022383.3, AC009131.6, AL354864.16, AL121900.26, AP000212.1, AP000134.1, AL031281.6, Z99716.4, AC009144.5, AC005015.2, AL137852.15, AP001207.3, AL035458.35, AP001753.1, AC026794.4, AL139022.4, AC009179.17, AL033383.26, AC090498.2, AC011472.7, AL162578.13, AL590762.1, AL117380.28, AF045555.1, AE006467.1, AC006088.1, AL096701.14, AL137881.12, AC011491.5, AC018828.3, AC005081.3, AC034193.4, AL110115.38, AB001523.1, AL023586.1, AL022237.1, AP000348.1, U91322.1, AL049591.12, AL133367.4, AC018808.4, AC091529.1, AC005666.1, AC011497.6, AL450339.5, AC004655.1, AP001718.1, AC005052.2, AC026866.8, AL136228.8, AC005793.1, AL139317.5, AL354720.14, AC004129.1, AL035461.11, AL161727.15, AF217413.1, AC007371.16, AL049539.21, AL008729.1, AC000353.27, AC003962.1, AC005940.3, AL158830.17, AF001549.1, AC004263.1, AC006441.13, AP000345.1, AC011811.42, AE006640.1, AL035086.12, AC004777.1, AC055120.5, AC002430.1, X02571.1, AC009477.4, AC006285.11, AC006597.2, AC018663.3, AC011479.6, AL139193.4, AC005692.1, AC009220.10, AC005907.1, AC007384.3, AC005049.2, AC004913.2, AC010328.4, AC005701.1, AC016025.12, U59962.1, AP003357.2, AC006345.4, AC006241.1, AL356805.5, AC004089.25, AC009247.12, AC005520.2, AC004910.1, AC027319.5, AC011495.6, AC008126.9, AC008521.5, AC005231.2, AC006449.19, AC002554.1, AL138720.19, AC011485.6, AL138875.8, AC008747.5, AC002994.2, AC003029.2, AC005291.1, AC006430.22, AL121712.27, AC078962.30, AL359082.16, AC004647.1, AC002429.1, AJ277546.2, AL133351.33, AL355102.5, AL391827.18, AL137140.12, AC004812.1, AC005098.2,

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HSAXA83	493	545051	1 - 635	15 - 649	

1441

HSDE95	498	664502	1 - 560	15 - 574	R63023, Z39624, F02373, AA993978, R66723, R67603, R59136, R80928, AA133775, AW874480, T48888, AA228698, AA368546, BF525711, AA115592, AA328299, AA486747, BG001652, AJ132502.1, AL034397. 1.
HSDEZ20	499	135228 7	1 - 781	15 - 795	BE881136, AW005333, AA631227, AA143192, AV707034, AA181022, AL301959, H98648, BF507561, AU143221, BF514388, AA594850, AV681894, AA287457, AI393857, N75788, BE044258, AA211849, F06608, N22567, AW450628, AA563681, AW195766, AI915322, BF701252, AA186657, AA992992, AA143136, AI302352, BF035111, AA631048, AV706818, AI341927, AV703142, BF446906, BE693540, AW961036, BE676990, AI870902, AV744251, AV749732, N75929, AW887695, AA973384, AA160641, AA338837, AK024037.1, AL359596. 1.
HSDFW45	500	589974	1 - 1728	15 - 1742	AL354891.11.
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HSDJA15	501	795252	1 - 1429	15 - 1443	

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HSDJ182	502	460602	1 - 448	15 - 462	AW594636, AA610164, AL050309.4, AC011445.6
HSDJL42	503	103647 1	1 - 2527	15 - 2541	BG260294, BG260369, BE564562, AW138350, AA035736, AL377064, AA456520, R53655, R53544, AA053788, BF924748, T10268, AL124831, R34409, BE149848, R15018, T80356, AA232756, AL141245, R39046, AA232126, T10269, AL453516, R41458, R48947, AW964468, AV702035, AW975618, AA809122, AW966330, AV718692, AW973474, AW973465, AV724520, AL535686, AV720533, C14331, AW973445, AW959799, AV718489, AW966333, Z21582, AW966386, AW960483, D51221, AW973307, AV720150, AV718427, AW949629, AW960465, AW960553, AW965158, AL557751, AV720731, AW966059, AV722801, AW973541, D58283, D80522, AW949645, AW966388, AV720729, Z30160, AW959570, AV721386, C14014, AW966531, AW978634, D80133, AV720151, AV699550, AW961136, D52291, AV720211, AW949634, AV719822, AV691387, AW973488, AW960454, AW966400, AV720616, AW966032, AW973330, AV700357, D80024, AA305578, AW949632, C05695, D80188, AW959202, D80248, AV718707, AV719557, AW966331, AW966398, AW959136, AV700889, AV696294, D57483, AW966062, AV719783, AV718931, AW960534, AV720464, H67854, AW966399, D80043, AW966343, AW952839, AW965177, AW966043, D59859, AW960532, AW964532, D80439, D58246, D81030, D80247, D51799, AW966369, D80251, AW973490, AV727418, D80157, AW975623, AA305409, AW966342, AV692290, AW950117, D80166, D80212, D80268, D80366, D59889, AW975613, D51423, D59619, AW978661, D80210, D80240, D80253, AV701839, D80219, AV719945, AV720088, AV719391, AW973447, AV719324, AV718938, D80064, AV718633, AW975605, AW966378, AW950578, AV720878, AW966368, AW959582, AV699447, AW966397, AW958993, AW949498, AV723927, AV699866, AV699715, AW965176, AW949653, AW949656, AV726330, AW949630, AW949631, AW949643, AW949618, AW949642, AW949657, AW949655, AV726423, D59551, AV684481.

HSDIM31	504	491112	1 - 547	15 - 561	AV694084, AV689813, AW966029, D80022, D59627, AW966332, T11417, AW966054, F13647, C14389, AV655880, AW966380, AW949633, C16955, D45273, D59317, AW966053, AV720291, AV700229, AW966075, H67866, C15076, AW966065, AW9660520, AK026158.1, AF131815.1, Z82022.1, AB028859.1, AB002449.1, AF058696. 1.
HSDSB09	505	130149 8	1 - 795	15 - 809	AA426010, A1986451, BE856226, AA773781, A1699994, BF477477, BF929123, BF526671, BF341281, AW020695, BF929118, BF966870, BF966816, BF966822, BF342126, AV726843, AC018616. 5.
HSDSE75	506	545057	1 - 1137	15 - 1151	BF432333, A1861851, A1240993, A1795956, A1074484, A1640759, AW006868, AW241621, BF592070, AW271387, AW614840, AW450466, AW243423, A1244694, A1640517, BF431431, BF431530, A1439169, A1613108, A1915938, A1984796, A1245393, AW300335, AA931466, AW235983, AC005722. 1.
HSDZR57	507	651375	1 - 294	15 - 308	AW378251, BF349814, AA687791, BF739001, AW378183, AA661723, H61383, T88677, H62404, AA443169, AW339864, AA458622, AA252063, A1129690, AW960791, AB006755.1, AB006756.1, AB006757. 1.
HSHAX21	508	612823	1 - 1972	15 - 1986	BE255995, AW473473, AW206723, BE312252, A1571368, A1810895, A1479711, A1656582, BE676619, A1492370, A1929750, A1762058, AW271956, BF591321, BF434884, A1500262, AW612319, AW085870, A1627969, AW168428, BE796769, A1767097, A1205848, AA632229, A1565786, BG033526, AV729047, AA876257, BE563237, BE905450, AA478285, BE257238, BE878838, BF664024, AA641693, AA478343, BC002907.1, AK000519.1, AC008755. 6.
HSIAS17	509	135219 1	1 - 1767	15 - 1781	BE379784, AL522216, AL520172, BF439334, A1652855, A1766309, BF512139, A1635715, AW299533, AW299897, A1129966, AW411210, A1624534, A1925109, A1803484, A1804159, BF184613, AA279212, A1609083, A1969459, A1860837, AA879465, A1183591, AW104990, AW316983, AW474646, AW630619, A1955714, AW409582, AA678827, BE139077, AA766602, A1431314, BF087963, AA081236, AW194027, BF701425, A1521521, AA588351, A1923638, A1155980, N39554, AV686756, AA769352, R78080, AW613876, AA259257, R22218, AA443811, AA969814, AA729654, R80114, T60532, A1969030, AW572611, AA259256, R80005, AW805183, BF592136, T51990, BE972627, Z38832, R23587, R24524, T52102, AA371263, A1564179, A1783565, BF700820, BE619819, AA447188, AK001845.1, A1136705. 1.
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HSICV24	510	135224 8	1 - 1396	15 - 1410	AL050277.1, AK000614.1, AL389939.1, AL359622.1, BC004529.1, AB055315.1, AL512733.1, AL133075.1, AL136768.1, AL117457.1, AL442082.1, AL136892.1, AL050138.1, AK026592.1, AC010374.5, BC001967.1, AB060912.1, AK026855.1, AL110225.1, BC002643.1, BC004265.1, AL512689.1, BC000714.1, AF211847.1, AF217991.1, AC023880.5, AL133560.1, BC003687.1, AF219137.1, AL512719.1, AF090934.1, AB060826.1, AK027096.1, AB048953.1, BC008899.1, AB050510.1, AK026647.1, AL133640.1, BC002798.1, AF225424.1, AK026541.1, AK026959.1, AK025414.1, AK026947.1, AK026526.1, AK027204.1, AK027213.1, AK025632.1, Y14314.1, AK026927.1, AF260566.1, BC005678.1, U80742.1, AL137480.1, U91329.1, AJ012755.1, AL133112.1, AF207829.1, AK027116.1, AL136799.1, AB055361.1, AF078844.1, BC001418.2, AK024524.1, AL136928.1, AK027081.1, AF097996.1, AL162008.1, AB048964.1, AL117583.1, AB063046.1, AB060908.1, AL137459.1, AK025431.1, AL117585.1, AK027200.1, AB055368.1, BC007680.1, AB052200.1, AK025524.1, AK025484.1, AL136845.1, AL359618.1, AL122093.1, AL133113.1, U42766.1, AL122123.1, AL080124.1, AL583915.1, AL512750.1, BC004244.1, AK000618.1, AB063070.1, AL110196.1, AK026353.1, AK000432.1, AK000137.1, AK025339.1, AC026464.6, BC004951.1, AL050172.1, AB060916.1, AL162006.1, AK027160.1, AB047904.1, AB049758.1, AK026631.1, AL137658.1, AY026527.1, BC006807.1.
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HSKDA27	515	135240 9	1 - 4398	15 - 4412	BF338364, BG253437, BG122685, BF037455, AW303375, AW173315, BF037378, BG120262, BG117983, BF915045, BF057308, BG252401, BG034853, BF793365, AW379378, BF826037, AA570507, BF915582, BG122734, W07328, AA600736, A1971935, BE697573, BE313814, A1090486, A1751258, BE839359, BF447303, AW631492, AA625303, BF513067, A1609700, A1768270, A1751257.

HSKHZ81	516	130710 5	1 - 955	15 - 969	BE939504, AA417652, AI751036, BE378218, AI652363, AI971415, AA599207, AI371013, AA024968, AI147536, W55850, AA063585, AW794702, AA446024, BE889110, AI828437, AI862133, AA421744, AI272646, AI148235, AA419609, AW005418, AA634323, BF883408, BF578271, AA416767, AA258414, AI083516, AI752526, AW024492, AI698032, AW957682, AI092202, AI191710, C05155, AA419525, AI218226, AI754332, AW794499, AA410929, AI936116, AI079893, BE272411, AA593295, AA455497, AI039656, BG035195, AA747741, AA774270, AA364833, AI350380, BF940413, T59268, BF197746, AI084698, AW800540, AA834031, AI673545, AW795817, AA978105, AA622501, AA032249, AA912802, AI432010, N66832, AI751035, AI754989, AI082183, BE178218, AI751086, N75819, N67061, AA971661, AA873147, AA478719, AA036654, T59227, AI538117, AA662437, BE765721, T66232, AI751085, AW674273, AA024662, BF197986, AI564218, AA319726, AA657729, N64555, AA852211, C03119, AI221431, AA455496, AA033678, C04206, AI520867, AA258397, AW867914, AW867908, AA382381, N24008, AA456579, AA936765, AI433202, AA446297, AW338252, BF940540, AI075349, D31528, BE839377, AI537292, AA382234, AI446798, BE839418, AA459088, BF724219, BE839363, BE773013, AI064722, AW375493, AW375513, AW375482, AW375483, AW375502, AW370152, AW134700, BF552435, AW375514, FI2285, BE772982, AW797394, BE839409, BE710069, AA299257, AI061637, BE773049, AW375497, H63649, AW805832, H29954, AI587210, AW836298, BE773047, H75893, BF985423, BF089372, AA610296, T73259, D30912, BE839372, BE934501, AW937287, AL531501, AI270416, AW376140, AW838930, AI886158, AA375571, AL134647, H94943, BG006581, AW964941, AA336003, AA410897, R94988, W47433, R64321, D31541, W39467, AV693669, T82080, W04350, AA384793, AW572523, BE693478, AW375499, BF569459, AA428478, BF001215, H43934, AA382233, Z20767, AA382380, BE157468, W16893, BE066790, AW384231, BE157596, H80974, R96403, BE814079, AA345211, BG153436, AV654605, BE157507, AW292030, H62182, AW384236, AI382511, BF674009, AA335755, H25902, W65400, BG169442, AV710284, T64640, AA994712, BF944442, BF725435, BF726055, BF917617, W67868, H71581, AA326037, M14036.1, X07577.1, M13690.1, M13656.1, M13203.1, X54486.1, X07432.1, AB062098.1, X07431.1, AB062097.1, AB062096.1, AI814274, BF869496, AI092236, AI275399, AI970748, AW381532, BF828729, BF828779, AI355259, AA055367, AA582963, BF825322, BE158757, BE158812, BE182090, BE182079, BE140770, BF737235, BE182110, BF836665, AW238620, BF828691, BF828827, AA055699, BE711192, BE717546, BF737527, BE140771, BF094219, BE158774, BF826017, BF838537, BE939669, AC002389.1.
HSKNB56	517	548077	1 - 1320	15 - 1334	AV715380, AV705910, BG170454, AW300598, AW996981, AA669095, AA278335, AI797687, AI948608, AA464762, AW996774, BF036901, AI718165, AI129358, AA504439, AI765613, AA114888, BE702298, AA521311, AA114887, AW298550, AA504203, AA810071, AI051218, AI299755, AA804200, AI701050, AI694270, AI631949, AA974370, BF434357, AI890342, AA256836, AI129632, AI023212, BE709212, AI935316, BE702132, AV726168, BE702036, AA252310, AA831496, AA662808, BE169470, AA464174, D57415, AA705444, BE702013, AA280044, Z44155,

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HSLCQ82	518	135222 6	1 - 1462	15 - 1476		BF116042, AA454571, AW192766, AI278160, H24834, AI091291, AA456465, AI242593, AA098966, AI379014, H24785, AA921986, BF745395.
HSLJG37	519	101692 0	1 - 2112	15 - 2126		AI733659, AI792379, AI003110, BF931916.
HSODE04	520	906081	1 - 1356	15 - 1370		BF369719, Z99289.1, AK027151. 1.
HSPBF70	521	793744	1 - 1383	15 - 1397		BF338332, BG178189, BE298379, AW772433, AI640184, AI751243, AI206927, AI989675, BF816124, AI439989, AA136304, AI128437, AI640906, AA136410, AA129952, AA341541, BE046990, AW382204, AW614497, BE004682, AI804666, BF327533, AI751242, BF327534, AW382118, AW992082, BE004684, AI689235, AI675842, AI274910, AI678921, AW082362, T10108, AI014513, AI538135, N47608, AI141309, AA885897, AI797519, AA652696, AI193489, AA872954, AI201747, AI244946, AI685761, AI810996, BF222389, N89795, AI224610, AI309547, AA513392, AA877674, AA894705, AA905637, AI056500, AW188156, AI138677, AI432328, AW466885, AI420740, AW873600, AI459017, AI047844, AI762549, AI382011, BF980675, T03552, T30150, AA917939, AI005050, AI797790, AI927908, BE857274, AA156935, AI453114, AI047845, H20185, AI140769, BF347892, F20400, AA628898, BE888983, AA928421, H05737, AW189222, AI860596, AA642494, AW058508, T70036, C00014, AA357087, AA731862, BF528632, AA742201, AA993626, AW873561, R39978, AI423668, H16241, AA983866, AI952326, BE152468, AI135012, AW858522, BF084778, AI134110, AW577199, AW601637, AI134524, AW577201, AI045327, AI045494, AI042523, BE927373, AW577192, AI045328, AI047163, AI042420, AI042468, U46344, AI042519, AE006467.1, AI031709.12, AK024842.1, AI136764.1, AI136762.1, AI133053.1, AI122101.1, AI136763.1, AI136758. 1.
HSQE084	522	130670 2	1 - 917	15 - 931		BE874396, BF210667, AV700682, AI271550, AI753304, AW082138, AV745382, AA809220, AW081079, AI879695, AV746084, AV753894, BF576504, AI879318, AI264068, AI219556, AV746036, AW973033, AA455733, AI382746, AA431230, AA548778, AV696126, BE673279, AW386283, AW608255, W78099, AA432251, AW608247, AI344174, AI344234, AF100751.1, AC009948.3, AI109755.14, Z62799.1, Z64678. 1.
HSSAJ29	523	630636	1 - 1030	15 - 1044		AUI118451, AI040060, AI222417, AW274713, AI799566, AI927599, AW316768, AI432204, BF507740, AI145007, AW275309, AI221808, AI251922, T77427, AI701846, T31064, AA970391, N69324, BG056871, AA325268, AW964700, AA377871, Z44814, R39528, AA757992, AA969668, AI282347, BF340244, R01659, C01260, Z40602, BG251489, AA371729, AA371555, H39944, AA078017, AF035281.1, AC004890. 2.

HSSDX51	524	56879	1 - 1129	15 - 1143	BF727258, AI792073, AI791928, BF088585, BE503986, BF736863, BF930592, BF527664, BE503764, BF727075, AW206230, BF849175, AA317765, R60584, AU123536, H22857, AI694498, F03192, R05669, AA365484, AW953971, AJ276171.1, AJ279016.1, AK001182. 1.
HSSFT08	525	58978	1 - 777	15 - 791	AA602964, AA609200, AI133255.13, AI157879.7, AL009030. 15.
HSSGD52	526	135234 3	1 - 2411	15 - 2425	AU140435, AI609706, AU118420, AI831837, BF529529, AI54814, BE786730, BF984481, BE872435, BE899402, BG179330, AI479884, AI982533, AI690830, AI346254, AI828401, BF094552, BE881525, BF094556, BE669959, BG037013, AW471268, AI561157, AI638805, AL037237, BE855637, AW296244, AI566243, AW675774, AI401405, AW673452, AI476445, AW001226, BF679313, BG057709, AA127685, BE907977, AA861929, BG260609, BF237821, AW956800, AA447921, AI571901, AW589479, AI766919, AI473830, AA938585, AU144989, AI262410, AA559052, AI446187, BG008928, AA917796, BE503565, AI275823, AW470299, AA127785, AI861789, AI167155, AW008965, AA905576, AI167659, BE218804, AI493520, AI281278, H99336, BE710637, AW205944, AI752329, AI752330, AI765810, AV653987, W52643, BF946032, AW168159, BF945858, BF316720, N26442, AA972078, AI817934, AI264423, W45166, AI557365, AI264431, AI288175, BE549758, AA442622, AI824617, AA919004, R70430, AA857204, AI368414, BF593079, AI418025, BE898318, AI262064, AA678751, BG057197, AI084548, W44908, H42841, AI827422, BE71829, AW449397, R48178, N93753, H72494, AA339568, BF108797, BE711822, R44778, BE091331, N88020, R48179, BE003856, AA678750, BE717116, AA837786, AW452952, BE828508, BF663442, AA975074, R19112, D11951, AI391505, BE814402, AI424232, AA436865, BF765542, AI420371, R82965, AW511561, AA541734, BE774069, AI867545, AA367966, AA385530, AA732924, AI371313, BF740054, AI828905, BF957657, H53943, BF764296, BF742191, T10746, F31373, AI559802, R09272, BG116091, R69447, AA303616, BE301258, W78796, W52012, BF956541, T07614, AW439006, T75428, BF917390, BE179163, AI086470, BF821360, BE938534, AA577454, BE301248, AI869470, AU076647, BF001674, AI086839, W94113, U94831.1, AI136295. 3.
HSSGG82	527	618535	1 - 1529	15 - 1543	AW964177, BF663662, AW603820, AI884560, AA398834, AA034137, BE503763, AW613529, BF509801, AA378851, H86275, H84069, BF346487, BF754228, AA327575, AA421165, BF686426, AI825151, BF476556, AI700323, AI591094, AW206900, AI948671, AI695979, AI632290, AW204774, AW134977.
HSSJC35	528	130693 7	1 - 1160	15 - 1174	BE867020, AI478611, AW135035, AI796551, AI493335, AI763397, AI205153, AW452868, AW024931, AI770003, AI860167, AW300835, AW236836, AI039293, AA312699, AI033837, BE047902, BF196530, AI587364, AI700805, AI364782, AI631435, AW516669, AA461101, AA741034, AA310989, AA449433, AI671731, AI373338, BE464413, AI621029, AI989810, AI247252, AI478533, AA448924, BF092110, AK000413.1, AB058750.1, AI121845. 20.
HSTBJ86	529	753250	1 - 1752	15 - 1766	AA380166, AC008553.4, AF001572.3, AI354811.13, AF000802.4, AC010591.8, AI161897.6, AC012323.7, AC005883.14, AI359874. 9.
HSUBW09	530	413246	1 - 1007	15 - 1021	AJ991103, AI765351, AA703513, BF939824, AI925701, AW295389, AW976578, AI199421, AI422698, AI934983, BE501421, AI127932, AA703493, AW297092, AA677025, AA848037, AI422698, AI934983, BE501421, AI127932, AA703493, AW297092, AA677025, AA848037.

						AA814098, AW404152, AW904298, AW182186, AW197850, AA741121, AA651794, A1678148, AA906044, F18680, AA743764, A1632270, AW590435, BE045258, AA608892, A1654853.
HSVAM10	531	520328	1 - 419	15 - 433		BF513864, A1309114, AC008583. 5.
HSVAT68	532	637680	1 - 1141	15 - 1155		AW839808, AA077633, BF919965, AC008171.3, AF041056.1, AC004089.25, AC005081.3, AC005015.2, AB006629. 2.
HSVBU91	533	596868	1 - 713	15 - 727		BF541621, A1926957, A1741909, AA534993, A1435345, A1803123, D82268, N34976, AW167331, A1093828, BF037342, A1140410, AA588188, BF349607, A1287515, AA844074, AA706579, AA759372, A1198783, H78775, A1261392, A1480026, A1027233, AA255439, BF800502, AA256930, A1928179, AW192517, AW961173, AA307508, BE143874, BE765577, BE766269, R11616, A1399819, BF752821, AW853138, AW352290, BF752819, BF752822, AW352288, AW352272, BF349404, AW352292, BF752834, AW352275, BE869822, A119319, Z99396, AW979284, AW970958, AW971965, AW975987, A1037094, AW979004, AW973808, A1036858, AW970564, AW969751, AW979210, AW972857, AW970978, A1036924, AW979140, AW972226, AW979252, AW976039, AW971981, BF868687, AW975126, AW973830, AW975247, AW969658, AW972933, AW972637, AW975922, AW971409, AW973715, AW971112, AW973821, AW972593, AW974272, AW979250, AW975952, AW971245, AW979238, AW976023, AW975607, AW975635, AW970043, AW969656, A1037639, AW973217, AW969885, AW973270, AW979204, AW970113, AW972884, AW973202, AW972695, AW973805, AW973213, AW972719, AW976515, AW975976, AW979165, AW971387, AW976510, AW971954, AW973770, AW972680, AW975975, AW969884, AW972943, AW969759, AW979083, BF592735, AW976982, AW970587, AW975876, AW973650, AW979175, AW973986, AW979064, AW975938, AW975016, AW975138, AW975966, AW975968, AW970921, AW969766, AW979116, AW972806, AW973987, AW975910, AW975943, AW972689, AW972706, AW973164, AW970097, AW973824, AW971964, BF588769, AW975904, AW974379, AW969752, AW976037, AW973718, AW973967, AW975933, AW979169, AW973207, AW979176, AW972882, AW973104, AW975028, AW969782, AW970868, AW972868, AW973985, AW973210, AW975648, AW971129, AW971403, AW973209, AW975971, AW972864, AW973219, AW972440, AW979178, AW972883, AW979081, AW973167, AW975162, AW973750, AW973185, AW971183, AW970110, AW972705, AW972827, AW973946, AW976012, AW979147, AW972823, AW970589, AW971259, AW971350, AW975261, AW971367, AW972685, AW972690, AW972817, AW979294, AW972371, AW975229, AW971968, AW972880, AW979085, AW979228, AW972699, AW979220, AW973190, AW974915, AW973088, AW975173, AW975955, AW974107, AW971429, AW969861, AW979219, A1036418, AW972808, AW973728, AW969839, AW972866, AW972417, AW973271, AW975018, AW975928, AW979201, AW972837, AW975964, AW972816, AW979090, AW969753, AW973997, AW975106, AW975168, AW974089, AW975025, AW971415, AW972711, AW972889, AW973804, AW971414, AW971413, AW975031, AW975914, AW972710, AW973740, AK024632.1, AB026436.
HSXCG83	534	944388	1 - 2098	15 - 2112		I.

HSXEQ06	535	101692 4	1 - 1584	15 - 1598	BG171665, BG109746, BE005933, BG026351, AL670834, AL793031, AW996511, AA481590, BF791148, BF110900, AA884278, AL554009, AA418164, AW966701, AL287582, N39228, AA177106, AA773834, AA233042, AL366763, AA417913, BF327654, AA232936, AW085026, N35014, R46292, FI2643, BF947218, AA953139, AV732449, AV660624, ZA3417, R54534, AL249382, AL817549, H53484, T34371, T32748, BE762828, AL268132, H26220, F08007, AA976991, Z39490, N72112, F03527, F04961, AA357869, H99278, F10258, R81334, R37424, AV734143, F07252, T74533, AA976568, R54437, AL433026, AW611733, N46671, H13274, N46079, AA481525, D62268, AA360677, H08120, R66918, R76039, BF830437, AA296802, BE811300, W00375, N43768, H93364, N46077, BE718145, AL559424, N72148, AA029181, AA743316, H08119, F36454, AA361446, AW890129, BE831170, AW063750, T77292, W00419, AL135691, AA057340, H86888, AA044960, H38947, BF891014, BE718142, D20601, AW293865, AF007142.1, AC024581.3, AL356017. 3.
HSXGI47	536	886200	1 - 1242	15 - 1256	AV760760, AW968156, AA737309, BE888245, AA640430, AA167792, AL163279.2, AC019205.4, AC027319.5, AC011811.42, AL449363.12, AC011445.6, AC020916.7, AC003663.1, AL162615.13, AL121886.22, AC005412.6, AL096840.25, AC007404.4, AL035704.9, AP001717.1, AC005098.2, AL356915.19, AC003029.2, AE000658.1, AC007739.2, AC010359.5, AC004867.5, AL022476.2, AC083884.6, AC005512.1, AC009079.4, AC004965.2, AC005932.1, AL031670.6, AC022217.5, AP002852.3, AC010605.4, AP001725.1, AC011489.6, AC008736.6, AC005519.3, AC009123.6, AL590762.1, AC004983.2, AL049776.3, AL138756.23, AC004166.12, AC008744.6, AC008474.7, AC005011.2, AC008812.7, AC011005.7, AL034420.16, AL137792.11, AC074121.16, AC016643.6, AL355392.7, AL121594.6, AC005089.2, AC020913.6, AL022721.1, AL449305.4, AL109827.8, AC006023.2, AC018720.5, AL035685.21, AL021155.1, AC010102.3, AC007731.14, AC079468.3, AL008730.1, AP001724.1, AC003566.1, AL391803.14, AC005736.1, AC020908.6, U91323.1, AL121845.20, AC005000.2, AC008745.6, AC008537.5, AL031005.1, AC026464.6, AL031727.42, AC011446.6, AC027644.9, AC008555.5, AC004821.3, AL031311.1, AF001548.1, AC009220.10, AC005280.3, AC016637.6, AP001716.1, AC011491.5, AC004491.1, AL022328.21, AC090947.1, AL135749.3, AC006141.2, AL354760.11, AL035659.22, AC027126.4, AC005102.1, AC020663.1, AL022323.7, AL050318.13, AL022322.1, AC008379.6, AC009155.3, AC011485.6, AC016644.7, AC008895.7, AC000353.27, AC005484.2, AC005274.1, AF053356.1, AL135927.14, AC007227.3, AC005500.2, AC008521.5, AC009144.5, AC007318.4, AC003288.1, AL161670.4, AC011461.4, AL133367.4, AC010320.9, AL022315.1, AC005800.1, AC002418.1, AC006101.3, AL391259.15, Z93023.1, AC006014.2, AC002350.1, AC009570.13, AD000092.1, AC007003.4, AC009131.6, AC018828.3, AC004929.2, AL138724.12, AL079342.17, Z99716.4, AC002425.1, AL121992.24, AL096791.12, AL049874.3, AL049759.10, AC005527.3, AC004883.2, AC018711.4, AL118520.26, AL121653.2, AC025593.5, AC006452.4, AL050335.32, AL139317.5, AL117348.25, AC006441.13, AL390252.9, AC019206.4, AC007151.2, AC010530.7, Y14768.1, AP000113.1, AP001709.1, Z93015.9, AC000003.1, Z84466.1, AC006329.5, AC004841.2, AC002312.1, AC018638.5, AC006345.4, AC002565.1, Z83844.5, AL451075.15, AC007374.6, AC003821.1, AL356481.16, AC004967.3,

HSYAV50	537	847358	1 - 2787	15 - 2801	AC005071.2, AC009412.6, AL139113.21, AC011247.10, AP000505.1, AL121819.6, AL033529.25, AC008738.6, AC003070.1, AC018809.4, Z93017.6, AF17635.1, AF196779.1, AC074013.5, AF129756.1, AC009120.8, AC008547.5, AC009086.5, AL034429.1, AL158830.17, AL353777.18, AC008481.7, AP003439.2, AP001748.1, Z95116.1, AC005057.2, AE006639.1, AC009309.4, AL355312.24, AC004951.5, AC009137.6, AL020997.1, AL049569.13, AL158206.8, AC026765.22, AL133174.15, AL445686.14, AP002348.3, AL160165.17, AC016526.6, AC068533. 7.
HSYAV66	538	686437	1 - 1393	15 - 1407	BF13680, BE742185, BE383304, BE741869, BF526599, BE619099, AL341487, AI971709, AI623222, AW593800, AW959076, AI983635, AI952164, AW275114, AI800042, AA977038, AW513859, AW273202, AW337946, AW273147, AI801910, BE463718, AA250733, AW072844, AI453134, AI818468, AI086791, BF329916, AW166266, AW300481, AI561259, AW103087, BE048584, BE907359, AW470887, BF063936, AI207341, AW235230, AA448721, AW206033, AW175624, AW193322, AW193240, AI128968, AW264492, AA410939, AI682412, AA455784, BF525380, AI631778, AW771868, AI669677, BE619620, AI128695, AA448630, AA456607, AW239315, AW195959, AI825128, AA327876, AI168173, BF376618, N79049, AA349394, AI470892, BF194812, D79030, AA902669, AI569983, AI682120, AA385255, AI052433, AI948815, W24199, AI735600, W24193, AI214684, AA770139, AI672486, AA769789, N91773, BF944570, C02034, AI955870, AC005222. 1.
HSYAZ50	539	102767	1 - 1083	15 - 1097	BF036117, AF126372. 1.
HSYAZ63	540	117753	1 - 3452	15 - 3466	BF918029, BF918027, BF732372, AW028622, H58607, BF935019, AW471489, AV707971, AV709796, AF168681.1, AC007378. 4.
					AV722966, BE388876, AV760983, AV762946, BF185935, AV762161, BF108823, AV759946, AV761323, BF064074, BF689470, BF001385, AI970338, AL046433, AI348109, BE349503, AI819289, AI090048, AW305162, AI857825, AA551911, AI963412, BF690404, N90883, AI652494, BG055077, AA311166, BE502539, AI200346, AI158746, AA502649, AW083258, BE551410, AV763075, W04340, AA150467, F29360, BF436259, AA040295, F21409, BF344822, R86673, AW206720, AI961780, W79500, AI831018, AA514281, AA609867, T67539, W79599, F25102, AA807108, AI351521, F36686, BE164504, AA056972, BF917215, F24355, W16820, AA513661, F30483, AI349360, AI805040, AA532766, AW590360, AI962009, AI817647, BE140360, AI720757, BG236085, T64334, AI400242, AI832241, R86847, BF741663, AI383420, N74174, T65686, N92928, AA584402, AW138172, AA297326, BE170117, AA359080, AL515041, AL515035, AL513867, AL515375, AL040243, AL513907, AL514303, AI540832, BE905408, AI433976, BG179993, BF883916, BG260037, AV681987, AW274192, BG257535, BG036520, BF793644, AL135661, BE048026, BF525438, AV657079, AI475371, BF037097, BG031815, BE964812, BG108147, AV715263, AL121270, AI702406, AI687728, AI863014, AL513911, AI439087, BE887488, BF340104, AV755678, BF812933, AL046849, BE048071, AV655645, AW071417, AI440239, BG036846, AL514627, BE876033, BG032208, AI224992, AI250293, AI497733, BE904178, BE877769, AL513553, BE047952, AI433157, BF968041, AL513597, AI064830, BE018334, AV757705, AV705644, AI802542, BE881061.

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HSYBG37	541	105631 7	1 - 1224	15 - 1238	BE898532, BF034673, BF337228, BF528632, BE857436, BE732588, BF527968, BE888983, BG033426, AW372231, AA156935, BF915018, AV690944, AI140769, AW068552, AI818102, AI870885, AA135715, AA928421, AL047844, AI927908, AI762549, AL047845, AI797790, AI005050, AA917939, AW873600, AI453114, AI420740, AW466885, AI432328, AI138677, AW188156, AW873561, BF980675, AW058508, BF770293, AA628898, AI094804, AI056500, BF820729, AI375863, BE857274, AW959629, AA905637, AI382011, AI860596, AA877674, AA513392, AI459017, W73121, AI242677, AI309547, BF819613, H16241, T70036, AA642494, AI675842, T03552, AI689235, BF919604, AI274910, AV748307, C00014, AI678921, AA993626, AI201747, AA742201, BF351125, BF770277, AW082362, BF914643, T30150, AI014513, R93245, H83130, AI538135, AI244946, AI952326, N45499, BF344569, AI685761, H05737, F20400, BF914807, AI094715, AI810996, AA320821, BF222389, H20376, H20185, H83129, T10108, AA370998, H12111, T70103, BF919644, AI800313, R47434, AI557606, AA299558, BF983106, BF347892, N47608, BF590090, AI141309, BF915129, AW385116, AA885897, BF917925, BF917920, N89795, AI797519, AA652696, AI193489, AA894705, T10109, AW189222, BF350004, BE829911, AI224610, AI423668, AA872954, AI207820, R39978, AI989675, AI439989, AI640906, BE046990, AI206927, AA136304, AW614497, AI751243, AI128437, AW772433, AI640184, AW385115, BF326281, W39052, AA595730, BF088390, AA731862, BF338332, BF111399, BF770143, BE767158, AA983866, AF302786.1, AE006467.1, AL031709.12, AK024842. 1.
HSZAF47	542	135217 2	1 - 1290	15 - 1304	AW298370, AI433823, AI239867, D62170, D61860, AF329839.1, AC007016. 5.
HT3SF53	543	884170	1 - 1912	15 - 1926	U69197, BE889880, AV070406, BG256172, BE379687, BE380123, BF691542, AV695897, BG259259, BF183831, BF984932, BE348298, BE813737, BF671812, BE837505, AL528978, BE966164, BF447947, BF540997, AA889669, AI983007, AA191622, BF131956, AI819766, AA427366, AI802592, BF217999, BG260695, BE042598, BF218184, AV700494, N31181, H16250, H11397, BF572925, AW952360, AA846829, AW874257, AI190464, AA157806, AI925182, BF952221, AI472734, BE888420, AA903609, AW169049, AW015713, AA033780, AA034036, AA609322, AI424168, BF219352, BE328721, AI333376, AW882963, AI362641, AW197207, AA910279, AI557117,

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HT5GJ57	544	129992 I	1 - 1759	15 - 1773	<p>BF975647, AW574516, BG259057, BE397179, BE396519, AW575080, BF795582, BF663664, AI521311, AW237047, AI446257, AI862389, BE559713, BF128855, AI573063, BF238156, AW296989, AU157608, AA811488, AA827120, AW338778, AI439638, AI250231, AI312540, AA633095, AV742373, AI343438, BE513368, AA604586, AI669176, AI149413, AW732709, AA723128, AW403042, BE269253, BE560794, AA722908, W57991, AI826124, BE246032, BG120258, AU138425, BE513265, AI865336, AI219708, AI589599, H23560, AA765412, AI589912, T61448, BE247378, BE560732, AW444827, AA594614, AA361096, AA648496, N34423, AV743440, W58075, N48728, AV742389, AA975334, AA731435, AI166766, AA810638, AW298682, AI919140, AI341517, BE245894, AI962720, BF062274, T30849, AW402333, AI982795, T25945, AA810222, AA807717, Z39117, AV756294, N48658, AW405561, AV724221, BG120887, AA593214, AW083122, AA639378, AI492348, H23535, AI656821, AF252613.1, BC009204.1, BC001609.1, AF252611.1, AF252614.1, AK002099.1, AF257135.1, AF252612.1, AF045555.1, BC006080.1, AC005081.3, AF086239.1.</p>
HTADW91	545	844835	1 - 1467	15 - 1481	<p>AI524277, AL525820, BE382621, BE906048, BE313348, BF311240, BF125870, BE314074, BE262971, BE261842, AW957565, AA434527, AI679032, AA429042, BF530443, AI269591, BF568093, AI751352, BF087452, AI926385, AW957563, AA427824, BF829853, BF207056, AI307680, AW751395, R73343, AA358983, AA985603, BF206540, BG029042, AA378137, AW016282, AA904900, BE767196, BE049123, AI538331, AI498177, AW084403, AW085619, AA428054,</p>

HTADX17 HTAE28	546	753289	1 - 1133	15 - 1147	AW081391, AA461497, AW439261, A1081131, A1764997, BE672411, AW057677, AA761398, BE221467, AW080458, A1244183, A1634014, AW193005, AW339212, AW516122, AW027659, AW067803, A1954056, AW571944, A1633339, AA772395, A1916888, A1683203, A1422341, AW025425, BE671235, A1147736, A1090554, A1380245, AW439080, A1282915, BF196022, AA351024, A1565421, A1089315, BE501181, BF476178, A1205166, AW270733, A1751353, A1135896, A1936764, AW024598, A1767080, A1016528, A1135895, A1707105, AA620766, R10091, T49864, BF920348, T97167, A1831497, AA399634, A1152339, AA865196, A1277342, R50357, AW081268, BE503733, R11029, AA617807, R11077, AA649308, R10190, BF589988, R53497, N50819, R77618, AA568975, AA399595, A1525780, R72870, W68569, AA351025, R71797, AA912795, R79394, AW768731, BF903645, AA894462, H13235, H24510, BE811970, BF568932, H30448, AA627105, BF206286, BF340605, AW067872, BC008853, A1133581, I.
	547	101829 1	1 - 1327	15 - 1341	AA446344, AA612751, AA298785, AA298780, AA298784, AA446524, AA298781, AA381170, AW195720, A1765273, A1817356, A1928166, A1283845, BE503396, AW081502, BE349083, BF059350, AA419437, AA758800, AW206944, AA933673, AW104261, A1627565, A1264565, AW469909, AA845240, AA332515, AL021453, I.
	548	396835	1 - 898	15 - 912	AI760170, A1150687, BF829200, AU158613, BF809865, AW273858, BE312404, BF316832, AU148518, BF314749, AU149720, BF315081, A1400198, AW062695, A1924082, BF314377, AW087415, BE047624, A1689214, A1684707, AA526748, BF315285, BE262228, A1566857, A1377786, AW167628, R65808, AA525309, R32753, AW663929, A1242434, BF206474, A1927229, R32754, A1956002, A1927230, A1701965, AU156607, BF349416, AW292033, A1368435, AA897436, BE314877, A1221593, A1612972, A1364630, BE185584, BF354201, AF352728, I, AF352729, I, AK022603, I.
HTEAF65	549	866485	1 - 549	15 - 563	AA778552, A1201364, A1150012, AA876180, A1223025, AW663435, AW304049, AW663514, AA978197, A1223459, AA903410, AA382504, AA864517, A1352610, AF012359, AA868778, AW102794, AW058243, A1513723, A1921248, A1513907, A1514015, F36855, BF792781, A1978703, A1538885, A1811603, A17131994, A1514721, A1736808, AA190341, A1118781, A1863466, A1250852, BE966927, AW827206, A1890907, A1049669, A1514867, A1538850, A1677797, A1039783, A1345688, BE011880, A1241744, A1571699, A1571909, A1560099, AW078650, A1866624, A1950100, A1690946, BG121335, A1932503, A1514689, A1036509, BF971336, A1446248, AW083804, A1081740, A1623941, BE965121, BE964576, A1647670, A1860027, A1514493, AA514684, A1491904, BE252769, AA693355, AW081242, BE965230, A1334893, A1514359, A1925196, BG110241, A1453328, A1513951, A1961286, BE963777, A1364135, AA767211, BG113188, A1824444, BE139128, AA937566, A1280747, AA744531, BE785348, AW131065, A1866798, A1565062, AW827290, A1524654, A1048323, A1866461, A1934039, A1579979, A1799158, A1048340, A1287489, A1681618, A1858310, A1690813, BE962857, A1440238, A1312428, A1724929, A1538764, A1927233, A1831308, H89138, AA844225, BE880209, AA580663, A1678446, A1513553, F34800, AW083750, BF680133, AW130356, A1310575, A1340603, A1633061, A1335363, A1538247, BG168054, BF764538, A1373276,

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HTEDF80	551	587326	1 - 1292	15 - 1306	AA952940, AA719708, D45556, AA709370, AW628803, AL766729, AW966053, AW978634, Z21582, AW975618, AV718489, D80949, D80227, AV699447, T03269, AW966531, AW966534, D80269, D80253, C75259, D51799, AV722801, D58283, AV719557, AW959628, D80166, AV699550, AV718692, AV719822, AW978661, AV699927, D51423, D59619, AV720731, AW960553, D59859, D80210, D80240, AV719188, AW959570, D80212, AW973307, AV719324, D80188, D80195, D81030, D80391, AW975621, D51079, AV720211, D59889, D80219, AV720203, AV723927, D80196, AW966062, AW966054, D80366, AW949656, AW949642, AV718440, AV719783, AV720028, AW965177, AV718800, D59927, AV718844, AV720464, AV718770, AW966013, D80043, AV724520, AW965158, D80378, AW966041, D80193, D80038, AW959582, AV744011, AW949629, AV721386, AW949645, AW949631, AW949643, AW949657, C14429, AV719468, AW949641, AW949633, AW949632, AW959597, AW966043, D57483, D80022, AW973447, AW949641, AW949633, AW949632, AW949618, AW966050, AV720812, F13647, D59275, D80241, AV700889, D59610, AV723097, AV718633, AW975605, AV720654, AW949646, AW949658, AV720791, AW949655, AW949654, AV742001, AV742667, AV701125, D80045, AV701335, AV701166, AV701043, AV701332, AV701017, AV701248, AV742048, AV701431, C14014, AW964488, D80134, AV701419, D59502, AV645389, AV742430, AV701154, AV699682, AW964737, AW959469, AV701443, AV745080, AV699669, AV701130, AV701149, AV645344, AV701422, AV719628, AV681510, AV681491, AV701415, AV701344, AW966560, AV701428, AW973470, AV681529, AV645343, AV721784, AV718674, AV701021, AW960474, AV681468, AV645383, AV645393, AV681528, AV681474, AV645339, AV681472, AV743601, AV681507, AV681465, AV681525, AV681495, AL390084.1, AF271371.1, X67155.2, D34614.1, D88547.1, AB033111.1.
HTEDY42	552	135219 3	1 - 740	15 - 754	AA393537, AL187279, AA889534, AW002667, AA421499, AW003587, AA421468, AA709184, AW772510, AA397830.

HTEFU65	553	543396	I - 1014	15 - 1028	AW072387, R83559, AI924465, AI364031, AW513660, BF361111, AA705541, AL162032, I.
HTEGA76	554	381995	I - 436	15 - 450	BF059486, AW293425, AI190540, AI201137, AI026778, AI016787, AA604883, AW172655, AA393061, AW09172, AC002456, I.
HTEGI42	555	908143	I - 964	15 - 978	BF792225, AW118908, AW956740, AA805770, AA578718, AA805757, AA808355, AA805773, N29112, AI760754, AI005113, AI204164, N21153, AI004282, AW956741, AI001990, BE564602, AI538204, AI1188040, AI301191, AA383104, AW182071, AI192033, BE168090, AA861920, N31710, AA887975, AA976455, BF812960, AI249323, AI564247, AI619607, AI961286, AI819976, AI567612, AI622033, AI554821, AI934036, AI538116, AI251434, BE964614, BF826445, AW105601, AI818980, AI926790, H89138, AI269862, AI288285, AW079075, AI280747, AW055252, AI621362, AV648430, AI590423, AW054931, AI538885, AI609556, AA455772, AI824764, AI670009, AI280637, AI277255, BE965432, AW168650, AI801523, AI955906, AI312428, AI916419, AI573038, AA527133, AI340603, AI801322, AI609409, AI871923, AI817543, AI680388, AI310575, AI591311, AI612885, AI340533, AV707062, AI134598, BE965121, AI582932, AI648663, AI801544, AW084869, BE895585, AI610362, AI784252, AW167776, AI569583, AI862144, BG258298, AI538218, AL039276, AW827285, BE965621, AI247193, AV738991, BF791806, AW148457, AI572787, AW022682, AI917253, AL121365, AI873644, AI969641, AI273142, AI281837, AI587143, AI571046, AW193000, AW081036, AI918655, AW167410, AW169039, AI589267, AI431408, AI913330, BF812961, BE048081, AI251221, AI653840, AW152459, BG255895, AI560099, BF812938, BF816042, AW131428, AV703695, BE910373, AI634224, AI452876, AW169653, AI497733, AI866798, AI917123, AI439443, AW198090, AI559752, AL036980, AI608667, AW945539, BG254754, AW834325, AI888953, AI654601, AW089350, AW084447, BF813196, AW193134, AL120853, AL134999, AI694157, AA420722, AI887308, AW020693, BE047833, AI334893, AI620015, AW827207, BG163618, AW169149, AW081449, AI866770, AL036631, AV682227, AI270055, AI285735, AI633125, BG256592, AI670849, BE964497, AI539808, AW192701, AW168718, AI340627, BF970652, AW150273, AI568855, AI887450, AI498067, AI625094, AI670002, BG121959, BG029829, AI890806, AI612721, AW081298, AI801325, AI446373, AI890223, BF884999, AL038605, BE965471, AI513687, BE963085, AI570884, AI923989, AI284517, BE972174, AI963193, AV714036, AI818977, AI269205, AW268253, AW301300, BE966505, AI349598, AV726784, BE966699, AI302910, BE879911, AW075207, AL036664, AA579232, AI543444, AI627360, AW087932, AV702147, AI345735, BE886728, AI136671, AC004006, BC004370, AI, AK026542, I, AF090943, I, AL133031, I, BC002733, I, AK026741, I, AL136754, I, BC004119, I, AF261134, I, AF056191, I, U42766, I, AB047904, I, AK024538, I, AL137521, I, AF091084, I, X82434, I, AB060825, I, AL050149, I, AF061943, I, AK026593, I, AL049938, I, AK000432, I, AB056421, I, BC001045, I, AL136845, I, AK027096, I, AK025967, I, BC006180, I, AK027164, I, AK026526, I, AK026631, I, AB060729, I, AL136622, I, AB062942, I, BC008899, I, AK026959, I, AL512765, I, AL122050, I, AK024974, I, AL050155, I, AL162083, I, AL049452, I, AK027204, I, AL133557, I, BC003548, I, AB052200, I, AL389947, I, AF260566, I, AL110280, I, AK026408, I, AL122049, I, AK000083, I, AK027213, I,

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HTEHR24	556	835894	1 - 1061	15 - 1075	AI419884, AI809484, AA824354, AF203447.1, AL136096.7.
HTEHU93	557	722254	1 - 724	15 - 738	AW665128, AA843468, AA918572, AA437250, AA759355, AW665453, AA436982, AF059244.1, AL109954.15.
HTEIP36	558	520468	1 - 738	15 - 752	AI695417.
HTEIV80	559	584798	1 - 1734	15 - 1748	AI349829, AI598077, AW936372, BE785942, BF954789, AI345549, AI340720, BE063579, AI252097, AI242057, AI032071, AI251249, AI793142, AV744706, AW514333, AI703269, AV710534, AW301368, AI652516, CI7730, AW888958, AW023124, AI336584, BF848969, AI685116, BF752041, AW075887, AI818151, AW974025, AI254827, AI822052, AI872435, AW301750, AI873822, AI921101, AA954995, AW268051, BE175422, AA446110, F16640, AI087951, AI191894, AI635355.

					BF931047, AA383566, AI377100, AA777615, C03348, AW268787, AW513247, AA587929, AA489231, AA832402, AW614777, AA402308, AW665144, AW795537, AW572610, AW956753, AW339583, AI868494, AW043812, BF513880, AI422008, BG006598, AV713025, AV648638, BF222519, BF957535, AI095021, AI803354, BF762181, AW838167, AI051341, BE891786, AW955404, AW088343, AA359513, BF594779, R81942, AI627336, AA771958, AA862135, AW853664, AI249995, AW867766, AW936566, AI570164, AI493146, AI036364, AI038713, AW264200, BF475948, AI824585, AU159276, N68060, AL046289, AA468571, AW102963, BE149642, AI245554, BF338824, AA406181, AA766076, AA826143, AI054162, AA804482, BE749129, AW016003, AI110348, AA584498, AI621138, AV690362, AA992185, AV691305, AI308534, AV695638, AV693309, AW157413, BF809037, AI369914, AV748735, BF576607, AI860800, F33837, AW516500, AV730830, AL162212.12, AC084239.1, AC018503.6, AC026189.4, AC006473.3, AC023480.6, AC018822.7, AC066587.4, AC005799.1, AC073387.4, AP001699.1, Z84470.1, AC004385.1, AC012558.8, AL450169.1, AC026341.17, AC007436.1, AC010739.3, AC002564.1, AL355916.2, AL356432.17, AL035594.7, AF279660.2, AL355520.8, AC016720.9, AC002429.1, AC007221.2, AL139115.5, AC007278.3, AP001671.1, AL357559.16, AL117191.6, AL355518.20, AC006500.4, AL109759.4, AC009247.12, AC016046.1, AL512283.12, AL157774.14, AL357041.11, AL139395.6, AC024095.13, AC006368.2, AC011745.4, AL035551.6, AF002997.2, AL160036.12, AL513011.7, AC005599.5, Z93403.1, AC020581.8, AF274856.2, AC009329.20, AC090042.1, AL357095.4, AL158196.24, AC002529.1, AL161901.18, AP000019.2, AL109620.4, AC004552.1, AL356916.17, AC009226.3, AL161912.15, AC011500.7, AB020869.1, AP002436.3, AC009961.11, AC016144.13, AC003084.1, AC004673.1, AC079175.24, U95743.1, AL022148.1, AL163206.2, AF207859.1, AC007514.5, AC025613.14, AL132670.18, AC060231.6, AC010450.6, AL353788.33, AC003677.1, M80340.1, AF196972.1, AL118523.18, AC007429.11, AL391986.12, AC005053.1, AL136987.11, L19088.1, AL031407.3, AL049831.2, AC023669.8, AL035688.8, U09115.1, U09116.1, AC004866.1, AC004757.1, AL389921.12, AC079178.20, AC073597.20, AC009478.4, AC009269.6, AL391595.14, AL161940.6, AL035633.18, AL158159.14, AC004200.1, AC002080.1, AF242452.1, AC073258.9, AF054599.1, AC016642.5, AC025770.5, Z93019.1, AL035464.20, AL121946.20, AC007037.4, AC018680.4, AC072063.5, AC002122.1, AL133474.9, AC006213.1, AF222686.1, AC020892.7, AP001713.1, AL161665.5, AC008277.4, AL031278.1, AC009289.8, AL031446.7, AC008250.23, AL159152.11, AL445466.9, AC012492.9, AC009479.4, AC025887.4, AL163642.4, AC006131.1, AL022144.1, AL138965.10, AC007611.5, AL499582.13, AC006840.17, AL136441.16, AC078851.4, AC004833.1, AC008174.2, AP001860.2, AL359332.2, AC002368.1, AL031117.1, AC010478.5, Z98950.1, AC005731.2, U51899.1, AC021017.4, AC034246.4, AC008935.8, AC009508.3, AL033538.1, AL050309.4, AL049741.7, Z98880.1, AL031681.16, L19092.1, AL022308.1.
HTEJN13	560	135227 2	1 - 1080	15 - 1094	AV701671, AI357650, BF438669, AI768345, AW007363, BE044135, AA757064, AI338828, AA813593, AI422179, AI198874, AI090848, AV717855, AI090870, R68504, AA974687, AV705429,

HTLM16	561	834058	1 - 517	15 - 531	<p>AI978569, AI694830, AI139115, T84300, R68213, AI129184, Z21304, AW014824, Z21445, AI557079, AF226731.1, AL390195. 10.</p> <p>AI651078, AW193716, AA833735, AI656090, AA939044, AI005061, BE550563, AA972135, AW173087, BE551605, AI807541, AW235553, AA769984, AI631437, BF755659, BF755660, AA910026, AI954833, AA442458, AW236934, BF478195, AW291899, AA807414, AW003815, AA436650, AI001919, W26260, AW070283, AW302924, AI344928, AI344933, BF968779, AI335449, AL031650.22, AL121751. 12.</p>
HTEPG70	562	834931	1 - 799	15 - 813	<p>AW001355, AA426091, AW182920, AI698237, AA844647, AW592578, AA436649, AA936263, AW072458, AA678521, AA42457, AC005789.1, AC005625. 1.</p>
HTGAU75	563	597467	1 - 1699	15 - 1713	<p>AI445595, AI453185, AV761152, D31303, AV735609, AJ224878.1, AJ240085.1, AJ240084. 1.</p>
HTGEP89	564	410582	1 - 689	15 - 703	<p>AV762334, AI300541, BG109719, AW663660, AA988368, AA927889, AA417006, AI206369, AA417219, AI005145, AI810124, AA723941, AA620800, AA917882, AA912169, BE927871, AA732367.</p>
HTHBG43	565	919911	1 - 834	15 - 848	<p>AA830144, AW196413, AW662711, AA346392, F01235, Z28908, AA704393, AV754716, AA602906, AI061313, BF804385, AA284247, AI609972, AW265614, AA491955, AW872574, AA715814, AW855528, AA552586, AW188742, AA622801, AA720774, AA502532, AA169245, AW238253, AI611533, BF870792, AI612070, AI301475, BF920612, AA528503, BE906142, AA558404, AA530958, AP003357.2, AP000555.1, AL049838.3, AC020906.6, AC003043.1, AL138878.10, AL031727.42, AC074338.1, AL355792.8, AF031078.1, AL022396.1, AL354932.26, AF030876.1, AL049637.43, AC005736.1, AP001116.1, AL133448.4, AL358777.12, AF243527.1, AP001712.1, AC016968.24, AC008736.6, AC073345.10, AC010271.6, AC007546.5, AC007687.16, AL035555.10, AL031678.2, AC010205.5, AC005940.3, AC002996.1, AC002565.1, AL162587.20, AL031228.1, AL109935.39, AL009181.1, AF168787.1, AP001331.1, AL031728.12, AC010150.3, AL157372.18, AC007731.14, AL049653.7, AC004821.3, AC005500.2, AL138759.20, AC009077.7, AC011527.4, AL022320.23, AL034405.16, AC018755.3, AC004611.1, AC021849.5, AL138837.12, AC007011.1, AC002300.1, AC007917.15, AL390209.1, AB038653.1, AL035462.21, AL391834.8, AL121928.13, AC006057.5, AC002432.1, AC009756.9, AC005098.2, AC009721.9, AL109947.19, AC010311.8, AC024563.4, AP001717.1, AL138752.5, AL009172.1, AC000035.2, AC002549.1, AL359494.17, AL008726.3, AL354766.17, AL353807.18, AL138743.5, Z84466.1, AL162424.20, AC073326.6, AP001748.1, AL118501.22, AC010768.9, AC005790.1, AC004222.1, AL035685.21, AC008946.6, AC009570.13, AL121972.17, AC004903.2, AC027130.5, AL049869.6, AC005215.1, AJ009613.4, AC009408.3, AC024561.4, AC005071.2, AL162426.20, AC003104.1, U80017.1, AL117382.28, AL132716.6, AC006581.16, AL122020.5, AC066597.4, AL031447.4, AC011445.6, AP001726.1, AL163279.2, AP001715.1, AC018828.3, AC005067.2, AC005288.1, AL137853.12, AC022383.3, AC010618.7, AL136295.3, AL133453.3, AL591398.2, AF067844.1, AC004032.7, AL034423.21, AC005971.5, AL353692.14, AL136170.12, AC006014.2, AC013467.8, AL117336.22, AC044797.5, AL158817.11, AC020552.4, Z83840.7, AL137077.31, AL031658.11, AC083863.2, AC007055.3.</p>

HTHCA18	566	908144	1 - 1804	15 - 1818	U82828.1, AC020913.6, AL390294.19, AC004253.1, AL132777.4, AC009086.5, AC011890.4, AL359397.3, AL022311.5, AC007993.15, AC000003.1, AC008427.7, AL513366.11, AC005939.1, U52111.2, AC010489.4, AL512666.6, AC005972.1, Z98884.11, AL137073.13, AC037475.9, AC011236.8, AC005520.2, AC011811.42, AC004089.25, AL137791.19, AP003465.2, AF064863.2, AC005031.1, AL031681.16, AL160163.24, AC009144.5, AL132640.4, AC016995.4, AC006208.3, AP001725.1, AC005089.2, AC011444.5, AF064861.1, AC000025.2, AL133373.5, AC002504.1, AL121891.22, AL358972.13, AF207550.1, AL133445.4, AC005368.1, AC006241.1, AL035659.22, AC011467.7, AL162417.22, AC005527.3, AC078962.30, AL139809.16, AC007991.7, AL096701.14, AC083884.6, AL121992.24, AL121594.6, AL136126.34, AC010458.5, AP002078.3, AC006966.3, AC004659.1, AC005086.2, AF229163.1, AC067722.21, AL031846.2, AP000257.1, AP002982.2, AC005081.3, AC005363.1, AC009068.10, AC007684.3, AL035587.5, AC010363.6, AC020626.6, AP001709.1, AL132639.4, AF190464.1, AC002301.1, AL133294.10, AC004778.1, AL137141.10.
HTHDI94	567	693652	1 - 1618	15 - 1632	AL290720, BG254585, BG251513, BG110633, BF526061, BE792285, AV704068, BF339939, BF338838, BG030014, BE615467, BF980189, BF308716, BE784543, AL533775, BF791036, BE880218, BF038786, AW955868, BG121135, A1741602, BE895986, BE264712, BE299196, AW886849, BF089485, BF089484, BE297034, BE311846, BF089488, BE270310, AL513740, BF671575, BE266974, BE299140, BF238947, D79185, BE294911, AW024422, AA401528, BE296524, AA417131, BF693821, A1333681, BF979464, W47348, AA280813, AW952740, AA905310, AA569922, AA573334, BE834263, AA902128, AW027880, AA570689, AL312759, AA976250, BE843385, AI092605, AA558902, AA151226, AI041784, AW262597, AA280806, N36166, W32108, AA151227, AA406299, AI090180, AA781961, AA115004, AI623995, AW239455, AI027447, AA065116, AI377228, N59607, AA451762, AI804317, AA724950, AA449952, AA450034, AA115005, AI186329, H10448, AA482977, AI242335, AW750196, AA453022, BF351185, BF091398, AI032607, AI804465, AA640751, BF307134, CI6610, AI149260, AA987598, AA781332, BF725960, AI804069, AA973798, AA452663, AA127134, AA872873, H82385, T86790, T82258, H10449, AV708991, BE122892, BG010794, F30722, BF955515, BE843374, BF742632, BF845452, T78950, W32213, W47452, AA541483, F06459, Z28571, BF091416, Z39388, AA297494, T86695, AI318411, F01234, AI424359, AA338139, BF515881, AA296988, T78898, AI285049, BE896826, AI278719, AA451764, AA808781, AA297421, AI991656, BF091818, BF091384, BE934690, AA661544, D31389, AA280856, AA280942, BF853987, AA064799, Z24822, BF826594, AA031579, AA298704, BF826595, AI670708, AW238447, AA494107, BE843391, AA296942, AA031458, AA297411, AA297354, AW748868, AA099261, AA098866, T83540, AA297420, AI675090, AA194682, BF091419, BE937871, AL533776, AA297201, D20890, BE937861, AI908416, AA897425, AA368017, BF755678, BE140557, BE871498, AW881778, AA411374, H70649, AA449811, F24096, AF125533.1, AF169481.1, AF091084.1, AK027319.1.
HTHDS25	568	772559	1 - 1047	15 - 1061	AI801504, AA385855, AA812703, AA349881, AI254831, AW293292, AI963714, BF674168.

					<p>AW967329, BE241437, T08386, AI521458, BF855114, AL357075.17, AL031668.23, AL358976.11, AP000067.1, AC004089.25, AL357519.19, AC005015.2, AL034417.14, AC004491.1, AC004962.1, AL133353.6, AC004634.1, AC022027.5, AC060231.6, AC004084.1, AB043547.1, AP000304.1, AL139390.15, AP000047.1, AL080243.21, AC004841.2, AL035685.21, AP000115.1, AC0008957.7, AL035684.25, AP001717.1, AC015982.9, AC020916.7, AL139230.25, AL096773.6, AL137073.13, Z85996.1, AC010386.5, AC005098.2, AC003010.1, AC004166.12, AC005488.2, AC012170.6, AC005972.1, AC008507.8, AC008569.6, AL049198.2, AL133354.14, AL1357507.9, AC008771.4, AB014077.1, AC011479.6, AC079171.21, AC004156.1, AL157823.9, AL356464.15, AL138976.5, AC002126.1, AL133507.8, AL024498.12, AC008766.4, AC020904.6, AL035073.7, U91323.1, AC005103.3, AL078633.32, AF047825.1.</p>
HTJMA95	569	706618	1 - 1636	15 - 1650	<p>AI608603, BE140256, AW872982, BF832764, AW352295, AI767967, AW085774, AW238519, AA863266, AW606064, AW117932, AI310728, BF105292, BF350121, BF825661, AW772195, AA865790, BE889218, AA864183, BF354847, BF832729, BF832728, BF354850, BF350182, BF354844, AI141812, BF354848, AI355569, AA595971, BF354846, BE350405, BF825662, BF353627, AW080463, BF353788, U75833, BF736474, BE141732, BE141331, AF193809.1, AF081497.1, AF284446.1, AF185277.1, AF219986.1, AF219985.1, AF219984.1, AF219983.1.</p>
HTJML75	570	104004 7	1 - 2748	15 - 2762	<p>AL521803, AL521804, AL535427, BE397366, BE562398, BF974996, BE561712, BE744093, BE397614, BE271237, BE562082, BE397567, BE275147, BE734376, BE409602, BE514409, BE561529, BE561508, AL535426, BE513947, BE269836, BE397322, BF025695, BE730298, BE397518, AW024974, AW303401, BE270550, BE277764, BE304392, BE747750, AW954868, AW954834, BE397865, BG104371, BF125819, BF892698, BE207701, BE296686, BE397490, BE271132, BE207727, AI274799, AW074233, AI679074, BE391918, AW732734, BE562087, AI499422, AI827575, AI928361, AA160606, BE267895, BF002414, AA315776, BE547421, BE644853, AV696893, AV684921, AW450819, BE268902, AI016059, AW249651, BF155203, BF437505, AL527262, AW079518, AI365272, AI338083, AA729126, AA831884, AI440443, AI283488, AI925468, BF237940, AI274761, AI983318, AW300875, R42025, AI527263, AA313959, BE268253, AI240111, R20845, R37892, BF970572, BF813074, AI187826, R33244, R64261, R33245, AA862592, AA984343, AW087285, AI984649, AA580394, BF902892, BF810667, AI795901, AI223980, H29720, R25583, AA283458, BF983060, AA928568, AW843336, AL513839, AL515041, BE894530, AL134259, BE048071, AI690835, AI920968, BG120816, AI952114, BG032704, BE904051, BG164371, BE048179, BF726198, AV696257, BG180034, AI491852, BG180996, BF882334, AI499463, AW301410, BE966388, AL135661, BF726504, AL045903, BG260037, AI539153, BG112879, AI349933, BF680131, BG058398, AW274192, AW148320, AW074993, AL036361, AV702623, BF970990, AI312152, AI873731, AW150578, AI345735, AV757943, AI868831, AW302992, AW238730, BG168696, BE966775, AI307708, AI608667, AV681731, BF924882, BG109270, BF812933, AW071417, AL513985, BE964876, BE964636, AL036146, BG249582, AI120854, BF794994, AL043326, BE047852, BF792469, AL036403, AI686926, AI521012, BF342070, BG114104,</p>

BG171779, AV755678, A1269696, AW071349, A1340582, AV735353, BG058208, AW087445, A1538716, A1872711, BF882343, AL045500, A1289937, A1564719, BG036846, BF343172, BG031815, A1349645, BE964812, A1571909, AV738991, BE048131, BG179993, BF526020, BF885675, BG112718, A1636445, BF817926, AL036396, A1620284, BE965121, BE048099, BF724691, AA613907, A1498579, AV732941, AW268253, A1433157, BG257535, BF971016, A1273048, AW827289, AW301409, A1349614, A1811344, BF055737, AW089572, AV706520, A1349004, AW827203, A1699857, AW162071, A1309401, A1312428, AW268220, BE172767, AW268251, AV682082, A1349957, A1922901, A1889203, AA508692, A1590128, AW118512, AW131954, AV682330, AW196141, A1612920, BG110517, BF968493, A1554484, AW103371, A1610756, A1912866, A1690312, AF191337.1, AB037827.1, AK026452.1, BC006807.1, BC008488.1, AB019565.1, AL122121.1, AL110221.1, AK000618.1, AL133080.1, AL359596.1, AK026865.1, AL050138.1, AF125949.1, AL110196.1, AL136586.1, AB063070.1, AB047615.1, AB047801.1, BC008387.1, S78214.1, AF078844.1, AK000445.1, BC001967.1, AL117457.1, AL133016.1, AL050393.1, AL136787.1, AL133565.1, AK025084.1, BC008365.1, AL117457.1, AL133016.1, AF090896.1, AL133606.1, AL050277.1, AB060863.1, AK026784.1, AL157431.1, AL122050.1, BC007021.1, AL162006.1, AF090903.1, AB063008.1, AL390167.1, AB049758.1, AL512719.1, AF106862.1, AF104032.1, AK026045.1, AK025958.1, BC003687.1, AL050116.1, AL049452.1, AF090901.1, AL122093.1, AL137527.1, AF091084.1, AB048953.1, AL133640.1, AL137459.1, AB056420.1, AL080060.1, AL359618.1, AF218014.1, AB055303.1, AL136789.1, AB060887.1, AF090900.1, AF111847.1, AB055361.1, U42766.1, AL136768.1, AK027868.1, BC003683.1, AL136799.1, AL133075.1, AL050108.1, AB060912.1, AL162083.1, AF090934.1, AJ242859.1, BC008417.1, AL136749.1, AK027096.1, AL133093.1, AK026608.1, AF207829.1, AK025339.1, AL049314.1, AK026741.1, AB060916.1, AL117460.1, AL442082.1, AB048964.1, AL389978.1, AK026855.1, AL136844.1, AL049466.1, AL133557.1, AF219137.1, AF146568.1, AL080137.1, AB056768.1, AF090943.1, AL096744.1, AL080124.1, AL050149.1, AL137557.1, BC002733.1, AL512754.1, AB063046.1, AK025772.1, AL359941.1, AK026744.1, AL359601.1, BC004556.1, AL136892.1, AL389982.1, AL049938.1, AK000137.1, AL512746.1, AB051158.1, AL442072.1, AL122123.1, BC001045.1, AB062938.1, AK000212.1, AF125948.1, X82434.1, AK026592.1, AK025092.1, AB060852.1, U91329.1, AL137283.1, AK026533.1, AL512718.1, Y16645.1, AB060908.1, AB048954.1, AK000083.1, AB055368.1, AB060825.1, AL110225.1, AL117394.1, AB060826.1, AK000652.1, AK024538.1, AK026583.1, BC006195.1, AK026647.1, AL353940.1, AB055366.1, AL117583.1, AK026532.1, AF225424.1, AL359615.1, AL049300.1, AK025491.1, AL133560.1, AL137550.1, AK026542.1, AK026927.1, AB055315.1, AK026504.1, AL117585.1, AB050510.1, AL136845.1, AK027113.1, AB047904.1, AL117435.1, AL133113.1, AL136928.1, AB056809.1, AF271350.1, BC007199.1, AL049464.1, BC008070.1, AF177336.1, AK026534.1, AL049382.1, AK026959.1, AB052191.1, BC002839.1, AF183393.1, AF097996.1, AL049430.1, AB056421.1, AK026086.1, AK026353.1, AB060883.1, AK027204.1, AK000323.1, AK000614.1,					
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HTLAA40	571	519329	1 - 942	15 - 956	AK000647.1, AL512761.1, AF260566.1, AK025414.1, AB060929.1, AL137463.1, AL122110.1, Z82022.1, BC008485.1, AK026528.1, AK000432.1, BC008899.1, BC004951.1, AB052200.1, AL137271.1, AK027164.1, BC008382.1, AL512684.1, AL137538.1, AK025967.1, AL136786.1, AL512689.1, AK025524.1, BC008983.1, AK024524.1, AK025391.1, AL359583.1, AK026947.1, AL122098.1, AB063084.1, AK000718.1, AL050024.1, AK026630.1, AL512765.1, AL162062.1, AK024588.1, AF348209.1, AL137648.1, AL353625.5, AL121656.2, AK026629.1, AK025632.1, AL080127.1, AB049892.1, AL133104.1, AK025906.1, AL110197.1, X72889.1, AL359622.1, AK026526.1, AK026480.1, AK026597.1, AK027116.1, AK025254.1, AL137521.1, AK025484.1, AW970655, AL037327, T63134, AA523995, AA437219, AI809780, AI313360, AA42282, AA868090, AA024526, AU156297, AI222715, AA024525, BF092179, BF092219, AA405033, AA412681, AK001866.1.
HTLBE23	572	902187	1 - 1202	15 - 1216	BE387950, BE391867, BF373101, AI024399, BE728010.
HTLEP53	573	634852	1 - 804	15 - 818	BF876683, AI755202, AI066646, AW613805, AA084609, AW769151, BE169870, AA601674, AI561210, BF926568, AW265614, BF826830, AI613389, AL042667, AL042670, AW130427, BF868994, AW471092, AV760019, AW576485, AI281818, AA225956, NG4587, AU157209, BF941382, AI340151, AI859834, AW328202, AV754716, AW501278, BG222269, AI955029, AL134440, AI799569, BG250286, AW518030, AW576437, BF725884, BE396138, AW974363, T05118, AA524616, AI732682, AW268329, AI192440, AA669741, AW166920, D58782, AI653493, AW238341, BE301068, AI955718, BF923179, BF526964, AW438850, AW438662, U95742.1, AC019205.4, AC027125.4, AL356299.16, AC007216.2, AC008649.6, AC005484.2, AC005098.2, AC005740.1, AB020868.1, AC008569.6, AL359091.10, AL136527.9, AC005527.3, AC005000.2, AC005529.7, AL121809.6, AC090883.1, AC006312.8, AC004166.12, AF250325.1, AL008726.3, AL139396.17, AC010913.9, Z85987.13, AL590762.1, AL121658.2, AI246003.1, AP001781.4, AP001694.1, AC004867.5, AL133312.3, AL513550.9, AC008507.8, AL022476.2, AC005520.2, AC068533.7, AL160163.24, AC011485.6, AF111167.2, AC002544.1, AC004702.1, AL158141.14, AC005071.2, AC007191.1, AC005229.1, AL357515.26, AC010412.7, AL161670.4, AF196972.1, AL135927.14, AC007227.3, AC083884.6, AC004089.25, AL445483.13, AF165926.2, AC009060.7, AL359235.3, AC002350.1, AC005952.1, AC007052.4, AC020558.4, AL035071.17, AP000510.2, AC007731.14, AL121586.31, AL354815.10, AC005500.2, AC006014.2, AC005015.2, AL161893.24, AC005726.1, AC004985.2, AL161725.13, AC002390.1, AL450265.11, AL353135.32, AL160231.4, AC026672.44, AC004466.1, AC060231.6, AL360227.17, AL117382.28, AL021397.1, AC083863.2, AC011487.5, AL158824.11, AC018638.5, AL031283.26, AL121761.5, AC004242.1, AL020993.1, AL512641.9, AL121936.17, AC005280.3, AL035587.5, AC020916.7, AC067941.7, AC009812.17, AC012476.8, AL136228.8, AP001728.1, AL354808.24, AL049561.16, AL352984.4, AP000046.1, AC010378.6, AC000381.1, AC006480.3, AC006023.2, AL050308.9, AC005531.1, AL049776.3, AP000114.1, AC008551.5, AL031680.20, AL391827.18, AP001360.4, AL354707.17, AF111168.2, AL031683.2, U89337.1, AC010605.4, AL035367.5, AC002546.1, AL138724.12, AL033521.2, AL031683.2, U89337.1, AC010605.4, AL035367.5, AC002546.1, AL138724.12, AL033521.2.

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HTLFE42	574	460583	1 - 698	15 - 712	BF059319, AL650872, AL341317, BE466535, AL650461, AL654221, BE552027, AL968418, AW002998, AW589844, AW593389, BF056905, AW274932, AW071622, AL979302, AL656601, AW138584, AL968442, AL968447, AW589880, AW003907, AA872876, AA922983, AL202932, AL627402, AW025629, AL655703, AW294061, AA398061, AL797621, AA833619, AL341052, AA992699, AP001579.1, AL163301.2, AL133499.2.
HTLFE57	575	135231 0	1 - 2234	15 - 2248	BE618638, BE740875, BF688973, BF967636, AW954531, BE742276, BF344608, BF966747, BF688501, BE314602, AV689075, BE881450, AV692451, AA402818, BE798735, BE392990, BF920872, BF439279, BG027910, AV698578, BF448645, BE250966, AA402161, AV686818, AL093167, AL150344, AL885410, U55991, AL160520, BE387679, AL523831, AL884689, AA018419, AA056110, AL080305, BG005830, BE394913, AL050824, AL141148, AW024987, AL870771, AW576097, N31844, AL809311, BF526976, AW71597, AL493689, AL395583, BG056680, AL200955, AL356543, AA419249, BF969738, AA306397, W72743, AA454906, AA041404, BE395222, AL143075, W58112, AL149739, AA436620, AA400067, BG056220, AA393477, AA861445, AW028724, AA573258, AL809303, BE671746, BE552382, AA259063, BE908638, AL220513, AA058572, W77922, AL087206, AA652366, D80807, W58172, AL074184, AL339724, AA132154, W31498, N72499, AL572664, AL933312, AL914114, AL219592, BE255290, AA649907, AA210767, AW970375, AW970296, AA970516, AW970376, AA594872, AL094655, AA733140, AA470469, AA631598, N23943, BG025452, AA041503, D80744, AA579798, BF967827, AW071229, T61071, AA534640, AA918880, AW016176, AA324492, AA657952, AV698775, AL244822, AV692171, H19641, AV691057, BF949226, D80745, AL032420, AV716910, AA534821, AA994420, AA725667.

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HTLGE31	576	103513 0	1 - 520	15 - 534	AA714179, AW051497, AI971919, AI094911, AW055123, AA293722, AI094408, AA631985, AL445222.9, Y17801.1, AI245937. 1.
HTLHV14	577	838460	1 - 1018	15 - 1032	AW182303, BF530991, AA885453, AA913620, AI024359, AI218809, AA436925, AA904573, AA729136, AA448181, AA431731, AI768931, AI138595, AA868685, AV721013, AI191602, AA970192, AI004977, H19402, AA496009, T19190, AI024060, AI015490, AA860370, AW081876, T05239, AA810634, AA609572, AA824562, AA789135, AA904853, AC005328.1, AC005545. 1.
HTLIT32	578	833906	1 - 1060	15 - 1074	AA430173, AA813342, AI688034, AI656828, AA431616, AI014589, AA446480, AI335754, AA759304, AW340541, AA912641, AA923430, AA431328, AA725624, AC020956.6, AC010616. 5.
HTLIV19	579	104634 1	1 - 964	15 - 978	H73550, AA715075, AA425924, AI792525, AA303049, AA715173, BF895531, AW086361, AV733366, AI348722, BE168680, BF880342, BF725844, BE464794, AI862231, AL033519.42, AL138706.9, Z82244.1, AC004000.1, L78810.1, AP002453.3, AL117382.28, AC004491.1, AC005399.19, AL354798.13, AC004867.5, AL022326.1, AC006160.9, AC004805.1, AC018801.4, AC022007.3, AL133444.4, AL356481.16, AL121751.12, AC008687.4, AC002369.1, AL353668.18, AC011495.6, AF279660.2, AL132640.4, AC004263.1, AC009077.7, AC005105.2, AL450169.1, AC025262.27, AC007425.16, AL050349.27, AC004887.2, AL022396.1, AC00160.4, AC018642.6, AP002340.3, AC074331.1, AE006462.1, AC002073.1, AC003070.1, AL031767.13, AL133153.3, AC007263.4, AC004882.2, AL050341.18, AC005921.3, AC007619.22, Z98200.8, AB003151.1, AC008050.6, Z92542.2, AC010305.3, AL157789.6, AC002300.1, AL020997.1, Z97989.1, AL023281.1, AL021707.2, AC079602.15, AC007225.2, AF243527.1, AC008267.6, AC007279.4, Z83840.7, AP001694.1, AL096764.11, AL031602.14, AC008895.7, AL391280.15, AC007073.2, AC005225.2, AL109614.28, AC008403.6, AL354808.24, AL138752.5, AL162430.15, AC008569.6, AL450104.14, AC007005.3, AL355392.7, AL133548.6, AL121997.7, AL034380.26, AL117352.12, AC009267.15, U91321.1, AL391827.18, AC022383.3, AC025438.5, AC091118.2, AC074013.5, AC002299.1, AL354797.16, U91326.1, AL034420.16, AC012384.16, AC022212.4, AL096840.25, AC005200.1, AC011489.6, AC008009.4, AL139317. 5.
HTNBO91	580	519313	1 - 286	15 - 300	AW194713, AI911340, AA601540, AI434870, AI810614, AA975093, AI026153, AW594027, BE502581, AW151600, AW196248, AW627679, AI669568, AA976768, BF437810, BF439076, AA975123, AI749464, AW966620, Z19502, AW196675, BE465426, BG120409, AA385366, BE221802, BE697980, N55869, AW631460, AK000497.1, AI136231.12, AB050415.1, AK000646. 1.

HTOAK16	581	560744	1 - 1452	15 - 1466	AU145310, AW274654, BF838423, AW139789, AW205436, AA017033, AU118838, T87405, AI143925, AI174470, T87300, AA019253, AK021714. 1.
HTODK73	582	526021	1 - 1005	15 - 1019	AI347130, AW027513, AW954660, AI660559, BF063427, BG230388, AI340321, AU155474, AI214222, AW006987, AI803717, AW301687, BE221184, AW016409, AA018238, AA019155, AI336534, AA015924, AI283525, AA921711, AA307210, AI090373, AA878131, AI269256, BF761125, AA017114, AI857978, BF229860, BG030487, AI368031, H84864, R84448, AW403382, AI367923, AW900223, AI284356, AI080385, AI350788, F29712, BE251142, AI536301, AA987803, BF761104, BF808782, AA017329, AA018635, BF593228, AA534529, BF851700, AL536302, W21988, BE910304, AA280994, AB031051.1, AL357033.19, AF205072.1, AK000551.1, AF104334.1, AK023410.1, AF187817. 1.
HTODO72	583	532001	1 - 959	15 - 973	AI401101, AI801654, AC005628. 4.
HTOGR42	584	838160	1 - 1416	15 - 1430	AA573067, H30513, AI266619, R20206, AW084004, AI064724, AW851828, BF031134, AA773890, AA507343, AL031295.1, AL355343.18, AC005031.1, AL354932.26, AC04797.5, AL356019.5, AC011994.10, AL034420.16, U80460.1, AL031281.6, AC022392.4, AC073657.5, Z59716.4, AF196779.1, AC009144.5, L44140.1, AC008440.8, AL049776.3, AL031847.17, AC010378.6, AL136418.4, AL139054.1, AC004797.1, AL353777.18, AL117382.28, AC005231.2, AC008521.5, AC002425.1, AC011446.6, AB023048.1, AL139113.21, AL355480.22, Z97196.1, AC008753.8, AL031685.18, AL160271.19, AL109952.15, AC004999.1, AC021012.5, AL355093.3, AL512883.5, AC007055.3, AF001550.1, Z95115.1, AC008745.6, AL021579.1, AL136304.10, AL121886.22, AC009086.5, AC003109.1, AC004953.1, AC005052.2, AL137229.4, AC005379.1, AC068724.7, AL135744.4, AL121890.34, AL589723.7, AC012170.6, AC005288.1, AC006538.1, D86995.1, AP000098.1, AC003007.1, AC009412.6, AL357497.17, Z83844.5, AL356575.8, AL031680.20, AL354735.14, AC007216.2, AL445071.14, AL136123.19, AP001710.1, AC008372.6, AP000901.5, AC025540.7, AF129756.1, AL355336.15, AP001717.1, AC008149.14, AC010279.4, AC008018.20, AC011487.5, AC003041.1, AL159997.14, AL080243.21, AF001549.1, AL135839.15, AC078962.30, AC008733.7, AP000504.1, AL132713.11, AL365505.15, AC005632.2, U62317. 2.
HTOHRM15	585	102853 8	1 - 1935	15 - 1949	AL118824, AA573022, AI754263, BE675104, AW272936, AI339372, BE349264, AA767823, AI379332, AI568638, BG057649, BE857312, AI870434, AI424042, AI203588, AI338543, AW080903, AI350585, AI827956, AI874102, AI304572, AW675567, AW029133, AA456303, AI885625, AA993567, AI028262, BF975457, AA808518, AW275811, AI086981, AA046802, BF478308, AV744983, AI869215, AA641617, AU157068, AI924628, BF594893, AW571905, AI146641, AI863164, AI214585, AI261778, AI492622, AW089250, BE207445, AA937376, AA830286, AA836878, W80372, AI023344, BE220743, AA418367, AI091921, AI885685, AA161459, AW134967, AA605225, AA725880, AW275980, AW248464, AA774650, AI991146, F09607, AA707150, AA593400, W17197, AA721238, AW073192, AA621167, AA908648, AI814647, R08844, AA290839, BE706675, AA100200, AA004650, AA285017, T65581, AA733113, AA405078, H19750, H53457, AA765557, AW383354, AI923502, AW615521, N95096, H50501, H24958, BF924331, H52806.

					BF71262, H02315, N92953, BE695264, N73135, BE695255, BE243599, N89778, BE695242, AI420513, AV710714, BF311141, AW672892, BE244250, BE410858, BE390798, BE265269, BE018715, BE730637, BE392884, BE407259, BE409678, BE796728, BE797085, BE279939, BG252804, AI990442, BE798385, BE877836, BG028222, W17255, H51332, AA101042, BE791799, BE259147, AA210904, AU129585, AA069873, H20075, BF025701, BE736857, BE890068, AA507302, H00417, BE799942, H19749, BE880605, BF676698, H46372, AI878952, AV709698, AI937600, BG026073, BE170116, AV749909, BE181361, W23659, BE181405, AA640620, T63652, AV727226, AA100199, H52769, AA046819, AA161408, AI743197, AI760050, BF663082, AI109658.5, AB049861.1, BC002801.1, AF283774.2, AK001511.1, AF112211.1, AK023385.1, AC004928.2.
HTOHT18	586	628300	I - 1485	I5 - 1499	
HTOIY21	587	665745	I - 1544	I5 - 1558	
HTOIZ02	588	826312	I - 535	I5 - 549	
HTOJA73	589	797108	I - 1280	I5 - 1294	AI963720, AI284640, BF668217, AV728425, AL046409, AI334443, AF330238, AV725423, AV762395, AA610491, AV760777, AV761106, AW265385, AV762098, AI270117, BF241967, AV761362, AV710066, AW979060, AW500125, AF074677, AI431303, AL138265, AV763670, AV762064, BF725504, AI305766, AV729881, AW303196, BF697673, BF337291, AV757607, AW193265, BG249643, AV740801, AW301350, AV761843, AV762505, AV763449, AV761489, AL138455, AW419262, BE049095, AV763971, AW472872, AA581903, AL119691, AI307608, BG059568, AW274349, AA490183, AW965008, AL037683, AI357901, BG109996, AL041690, AA720702, AW963497, AI046205, AI613280, AV759204, AV760486, BF683672, AA665330, BF677892, AL044940, BF680074, AW502975, BG059450, AV762092, AW974109, BF827410, BF541120, AI350211, AW833862, AV764307, AV760466, AV764329, BE139146, BG104686, AA682912, AV763540, AV735370, AI345654, AV756693, AV762111, AW327868, AV760937, AV763354, BE672637, AI754336, AI281881, AI457397, AV733830, BF970654, AV703682, AI345681, AV760042, AI890348, BE276880, AV738303, BF679304, BE049139, AV759172, AI355206, AV762959, AV762645, AI610920, AA587604, AA680243, AA491814, AL042853, AI801482, AU147104, AW073470, AA877817, AV763633, AV702857, AW410400, AI345675, AV763255, AV760057, AW088846, AA521399, BG222267, AV762397, AW953071, AV759362, AW238278, AV858127, H71429, AV759274, AW513362, AI860020, AV760395, AW662543, AV761786, AW408717, AF063563, BF680041, AW028429, BF915722, AV764578, AV764530, AW960468, AV762535, BF915247, BF030810, BF991286, AV764241, AL045053, AI754658, AV732891, AW503666, AA521323, BF965406, BF475381, AW501386, AW072923, BF915628, BF965007, AV725431, F36273, AI133102, AL042420, AW872676, AW996768, BF758600, AI064864, AW956640, BF691714, AV763847, AA468022, AW406755, AW975987, AI345157, AV762009, AI732120, AW513015, AW576503, BF793766, AA857486, AA569471, BG036665, AI133164, AA126450, BE350475, AV691147, AW974932, AI061334, AV759518, AI754253, AW020340, AV728928, AI538852, BF681576, AI623720, AI289067, AA613203, AI307201, BG179731, BE439761.

AW276827, AW021583, AL161997, AW270382, AL696962, AW956641, AV761745, AU145393, AA584201, AL254615, AW969629, BG171096, AW957076, BE253771, AW500684, AV759382, AU561060, AW872575, AW268300, AW576391, AL341664, AW438643, AV764398, AV729809, AL121385, AW679782, AW518220, AL370074, AL046457, BF724767, AW504669, D83989.1, AL445248.7, AF015149.1, AL163279.2, AC011755.7, U18394.1, AL139039.17, AP001216.3, AC020917.4, AF015151.1, U57007.1, U18391.1, X55925.1, X55926.1, X54178.1, AL135839.15, AF015148.1, M37551.1, AC008887.5, AC011440.5, U57009.1, AL136179.15, AC0073545.4, AC035149.3, X54181.1, U91322.1, AF015147.1, X54180.1, AE000658.1, U18395.1, AL136124.10, AC008525.7, AL513008.14, AC008848.7, AL355384.6, AC005082.3, AC018828.3, X76070.1, AP001037.1, U18392.1, AL161670.4, AF121781.1, Z85986.1, AF015156.1, AC005516.1, U02531.1, AL031904.1, AC009958.2, AC007043.3, AL359552.16, AL121890.34, AL355478.16, AC012492.9, AC009506.5, AL158832.13, X55927.1, AC021851.4, AP000842.4, AC011748.7, AC0073135.3, AC006458.2, X54175.1, AC004848.1, AF015157.1, AF068862.1, AC007681.3, U18393.1, U57008.1, AC004612.1, AC006131.1, U18398.1, AL445242.3, AP001732.1, AL353748.13, AC034193.4, U02532.1, AC004965.2, AC008623.4, AC018808.4, AC006392.1, X53550.1, U67221.1, U18387.1, AC003081.1, AC005212.1, AL049696.9, AC008080.1, AC010422.7, U18399.1, AL035423.4, AC004139.1, AF243527.1, AP000567.2, AC016025.12, AL162831.5, X55931.1, AL132780.5, AL158830.17, AP001224.3, Z94721.1, AC040160.4, AC005531.1, AL109919.18, AC004057.1, AC020559.4, AL117348.25, AL391415.12, AC034198.6, AL135927.14, AC007227.3, AC008687.4, AF126531.1, AL138724.12, AL356244.12, AC005081.3, AC007365.3, AL031680.20, AL021026.1, AC010792.4, AP000087.1, AL031670.6, AC023423.5, AL354674.5, AC004948.2, X75335.1, AC016691.10, AC073542.4, AC006367.3, AC011005.7, AL513007.5, AL136171.17, AL109804.41, AF223391.1, X54179.1, AL035681.13, AC007437.16, AC005933.1, D87008.1, AL133396.2, AL353807.18, AC012476.8, AC022384.4, AC011455.6, AC079383.17, AC006130.1, AC015853.8, AC006262.1, AL121655.1, AL109759.4, AC008764.7, AC004854.2, AL049776.3, AC005004.3, X55922.1, AP001708.1, AC007005.3, AC010103.10, AL590611.7, AL590762.1, AC010616.5, AL023494.12, AC007216.2, AF049895.1, U67801.1, AC010428.6, D88268.1, AF015153.1, AC004485.1, X54177.1, AP001694.1, AC005701.1, AL122015.17, AC004797.1, Z97181.1, AF045448.1, AL162713.19, AB041731.1, AC084882.2, AL049709.18, AC008616.6, AC016080.5, AL121949.13, AL138836.15, AC004041.1, AC012377.5, AC006254.10, AL135940.11, AL138784.30, AC009086.5, AC003109.1, AC005052.2, AC005998.3, AP001724.1, AL359435.7, AF064864.1, AF077058.1, AL096862.18, AL450339.5, AC006543.7, AL121899.37, AC012150.16, AL121972.17, AC002067.1, AL353739.4, AL355074.5, AC022383.3, AC023425.20, AL354676.10, AP001342.1, AC009311.3, AC020604.9, AL021978.1, Z94044.1, AL160175.5, AC008817.7, AF285443.2, AC023512.28, AC005037.2, AL109865.36, AL159140.4, AF252830.3, AF002992.1, AC024561.4, AL354798.13, AL035072.16, AL023799.5, Z81308.2, AC009039.6, AL139110.17, Z98745.1, AC007066.4, Z22650.1, Z69719.1, AC074000.8, AC072052.6, AC005908.1, AL135844.9, AC007256.5,				
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HTOJK60	590	545067	1 - 890	15 - 904	<p>AC027612.6, U95742.1, AL157938.22, AP002456.3, AC012351.3, AC007656.2, AL049757.14, AC006039.2, AC006207.5, AC005704.1, AP003438.2, AL135744. 4.</p> <p>AL079734, AL1613389, AA129746, AL267356, AW970571, BE048991, AL267450, BF902572, AL133083, AL085242, H07953, AL253376, BG029528, AL038606, BF876179, AL207728, BF868994, AL049709, AA832016, BG222875, AA720774, AW089016, AW995665, BE084668, AA565911, BF821897, BG015615, BF529925, BE256101, AL357823, N30205, AL249447, AL537800, AA632839, AL440117, T74524, BE244243, AA501867, BE000614, BE154781, AA502207, AA084609, AA599080, AL679759, AV760019, AA191659, AA515351, BF678165, AW069412, AL284092, AW265359, AA056177, BE387304, AV757069, BF131490, BE049021, AW970987, AW276678, AW303098, AA584756, AW021627, AL628859, BE893315, AL251034, AA912287, BE501593, BE139139, AU117926, AC084864.2, AC078846.2, AC004815.2, U51560.1, AL400877.1, AL445490.6, AC024082.6, AC007078.3, Z80896.2, AC012170.6, AL009612.5, AC005940.3, AL357497.17, AC022415.5, AC008736.6, AL023879.1, AC004520.1, AL009031.1, AP003352.2, Z95116.1, AL356095.11, AL135927.14, AC007227.3, AC068533.7, AC005071.2, AP001710.1, AC003007.1, AL035420.15, AL353807.18, AC018695.6, AF168787.1, AL359494.17, AC012384.16, AC009311.3, AL17336.22, AC005736.1, AC008784.6, AB003151.1, AL024498.12, AC005519.3, AP000553.1, AL135928.6, AC011472.7, AL133373.5, AP000359.1, AC022201.4, AC004000.1, AF036405.1, AC019206.4, AC008403.6, AC008626.5, AB000882.1, AC005341.12, AC002430.1, U67810.1, AC004867.5, AL109804.41, AC007384.3, AC009039.1, U89335.1, AL049713.20, AL020997.1, AL049776.3, AC008962.8, AL022238.1, AC007216.2, AC006329.5, AC027129.5, AC083871.2, AC005907.1, AC004166.12, U95742.1, AL138725.19, AC002326.1, AL132777.4, AC055740.17, AL356915.19, AC011446.6, AC008397.7, AL365364.19, AC009412.6, AC001227.1, AP001748.1, AC011452.6, Z83844.5, AC002476.1, AC011475.6, AC003101.1, AL136295.3, AL157912.5, AC011464.5, AC011450.4, AL138889.9, AL022476.2, AL138965.10, AC004878.2, AL356785.18, U62631.1, AL035587.5, AL354932.26, AC024085.5, AP001714.1, AC006312.8, AC009145.4, X55926.1, AC020917.4, AC002544.1, AL139099.2, AC005500.2, AC073136.6, AC002543.1, AL121943.22, Z93015.9, AL138822.13, AC004990.1, AL354928.9, AL121901.20, AC004702.1, AL121601.13, AC011491.5, AP001412.2, AL049869.6, AL159191.4, L44140.1, AC017082.4, AL035407.15, AF001549.1, AC004821.3, AC004814.2, AC018506.4, AC009131.6, Z82244.1, AC022083.6, AL162584.9, AC006333.3, AC005005.1, AL355480.22, AL161626.20, AC006367.3, AC011455.6, AL096701.14, AL049653.7, AC005874.3, AF134471.1, AC001231.2, AL021154.1, U91326.1, AP000688.1, AP000692.1, AC009996.7, AL117258.4, AP000687.2, AC005332.1, AP001666.1, AP000151.1, AP000152.1, AP003357.2, AC006275.1, AP000252.1, AC044797.5, AC005015.2, AL031311.1, AC009004.6, AC023105.7, AP000208.1, AP000130.1, AC005291.1, AL121834.20, AF250324.1, AC011490.7, AL031295.1, AC008812.7, AL353716.18, AC067941.7, AP001630.1, AL121881.35, AC004812.1, AP000313.1, AC004686.1, AL031005.1, AP001724.1, AC074121.16, AC007318.4, AL139002.18, AP001432.1, AC026794.4, AC006285.11, AC002558.1, AP000521.1,</p>
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HTPBW79	591	131783 5	1 - 1360	15 - 1374	AC007376.9, AC005632.2, AL138836.15, AC011484.4, AC009570.13, AP000247.1, AL391987.15, AL159997.14, AL031721.1, AC007842.1, AL133244.1, AC002563.1, AC005839.1, AC020931.5, AC016697.8, AC034240.4, AL031123.14, AP000212.1, AL136139.6, AC073897.6, AC007679.4, AC005821.1, AP002085.1, AC009079.4, AL451075.15, AC007283.3, AL033529.25, AC005098.2, AC005207.1, AL133284.13, AL390074.17, AL445184.11, AP000134.1, AC009331.5, AC084881.19, Z99716.4, AC008649.6, AF088219.1, AC006511.5, AC005871.3, AP001716.1, AC009510.9, AC007546.5, AL139415.10, AL021977.10, AC004824.3, AC0022308.17, AC009229.5, AC011811.42, AP000103.1, AF196971.1, AP001728.1, AC010654.8, AC006138.1, AC005378.2, AL389889.11, AL532387, AL532388, AL520598, AL534919, AL536351, AL529149, BE740155, BG031799, BE269797, BF984158, AL529148, AL537418, BF315754, BE891262, BE298901, BE409619, BE261844, BE296298, BF691759, BF316798, BE387294, BF316385, BE865498, BE279596, BG116442, BG115631, BF725854, BG236132, AL924354, BF058328, BE315264, BE279832, AW960909, AW953297, AJ921207, BG027736, BE391898, BF981073, AW089642, AW607100, AW083566, AA779231, BF950834, BF769481, AL536350, AI597662, W72124, AA757487, AI004378, AW474708, BF950841, AA779154, AW966051, AI815918, AA181149, BF214063, AW609985, AI719697, AA181148, NS2277, BE266550, BF514424, AA644552, AA315773, AV655765, AA657491, BE279156, BF997441, C05777, AA630867, AV647073, AA446396, BF512274, BF985404, BF894339, BE207304, AA768108, AI003424, NS3936, AI358817, AA302986, BF986382, AA575917, AW615772, AV747904, AW409761, BE870050, AI815721, AV710773, AA009415, AI362635, BE276831, BF750334, AA554868, AA088502, BF802327, AI648676, AI560267, Z40243, N32193, R37325, AW628445, AI831717, BF871083, BF813931, BG004621, AA563856, AA868751, AA088448, T69236, R12437, NS9026, Z44284, T58935, W77848, AA009696, R13448, AW241297, R37361, AI184854, T58875, BF872966, AA765983, AI383674, AA303060, N72929, AA296970, AV746892, R72050, BE934313, W38735, BF769484, AA027796, AA552128, AI423329, BE706063, BE074034, BE673575, AA323238, AA385759, AW610075, AW935206, AA365395, AA973951, AI474457, BE934455, AA350856, AA843692, BE926535, BG003907, AA302913, BF593049, T54203, BG003213, AW827234, AI961882, BF590312, BF531118, BG025715, BF341680, AA507090, AA873450, AI742493, BC000001.1, AF212229.1, AK027711.1.
HTSEW17	592	460579	1 - 638	15 - 652	AA779073, AI860913, AI028060, AI024955, BE549714, AW136463, R07163, AW612172, BF773051, AF007146.1, AF381980.1.
HTTDB46	593	812763	1 - 3045	15 - 3059	BF333492, AK025267.1, AK025111.1, AB020625.1, AC016572.5, AC022413.4.
HTWCT03	594	429618	1 - 1949	15 - 1963	AA429504, BE709846, N57518, AA279467, H09648, R41904, AA007236, BF764791, AW810272, AU119787, BE790560, BF589035, BF437720, AW135490, U74496.1, Z95704.1, AL078621.19, AP001761.1, AP000218.1, AP000340.1, AC004908.1, AC002055.2, AF270552.1, AB019437.1, Z96386.1, AK021903.1, AF017466.1, AF328497.1, AF035187.1, AF035188.1, AF327134.1, AF229518.1, AF328523.1.
HTWDF76	595	714344	1 - 949	15 - 963	AL528049, AL043219, AW088366, AW152013, BE779803, BE672597, AW243555, AI818186,

HTXAJ12	596	131081 4	1 - 661	15 - 675	AI653697, BE251084, AU160597, AU150608, AI871013, AA496891, AA428540, AA349190, AW249598, AI701503, AU151739, BE502287, TI8883, AI202674, AU152190, AW732070, AI376266, AW139928, AI299710, AI888510, AI658535, AW341396, BF976767, BF224111, AA912087, AA694485, AI887614, AI7658, AA422221, T33286, AI571236, AI299136, R56443, R51367, BF447467, AI367595, AI420610, AI825055, T70333, AA928620, AI681192, AI499499, AI197972, AA664995, BE045622, AI961711, AI184815, AA888827, AA768736, AI659770, AA292170, AI383839, AI888009, R51842, AA973896, AW470342, AI915171, AI989713, BF802487, BE799943, AI275745, AI934660, Z39039, AA634437, AW137356, F04023, AI762348, AI253211, AI824874, AI136295.3, BC004159.1, AK001435.1, AF006264. 1.
HTXCV12	597	135221 3	1 - 1120	15 - 1134	AA456896, BE783654, BG251027, AA768759, AI806785, AC083866.2, AC011005.7, V00584.1, K01562.1, AL035087.20, U84680. 1.
HTXDW56	598	695765	1 - 1569	15 - 1583	AI014551, AI379840, AA928131, AA463863, AA463357, AI360362, AI553741, AI933132, AA682260, AA437378, AW612124, BE939238, AC017099. 11. BE891580, BE874295, BE272309, BE905589, AU123343, BE790068, BG171568, BF797209, BE746860, BG027340, BE866834, AI765620, BE394238, BF978180, AV691685, BF131943, AW993028, AA725071, BF701185, BF029881, BF724883, AW271710, BE855449, BG122640, AV692294, BE549980, AI916562, BE936367, BE936346, BF130329, BF244421, BF088035, AI634990, BF088014, BF088012, BF088026, BF449073, BG165351, BE936324, BF593983, AI654165, BF939873, AI991405, BF592056, BF088032, AU151546, BE936318, BF923670, BF088037, BG250837, BF088024, AW750352, AI983985, AW299864, BF088028, BE936364, AI670830, BF088019, AW750348, AI570128, BF197216, AW168930, AW009948, AA704525, AI749744, BE349529, AW009166, AA861614, AI955276, AI492455, AI676055, BE549294, AI276897, BF898194, BF880528, BE936352, BF102773, BF983492, AI681128, AI796805, AW275120, BE468207, AA430567, AI659635, AW419101, AA890343, AW167370, AI635116, BE221529, AI361022, AI700668, BE858834, AW614823, AI968287, AW276391, AW592400, AI935478, AI089414, AI955265, AI912091, BE857580, BF573804, AI718821, BE349946, AI935972, AI216100, AA699534, AA030011, BF971066, BF038581, AA587495, BF821491, AI025329, AI300305, BE304656, AI342565, BG012643, BF848195, BF923020, AI308169, N38817, AV695789, BF436974, BG171706, BF898192, AI298732, AA704532, AI628899, AI018477, BF572796, AA115429, AW752990, AI334626, AA774557, BE302369, AA045856, BF088010, AW752951, AI160398, AA628480, AA55219, AW752948, AA189132, AA780575, AI983713, AW752946, AI686341, BF923688, AW512904, AW752986, AI350088, BF108993, BE074717, AI917769, AI263986, BE868265, BF446418, AI131166, BE677404, AI207172, AI347097, AI094833, W31093, AA216738, AA922079, BF339506, BF062926, AI095199, BF928253, BF308118, BF240462, AA911845, BF880533, BF923693, AI356898, R24001, AI827291, AI251444, AI828631, BF689464, AA190469, AA774568, BF218904, N66175, AW827086, BF923018, AW897464, BF801661, W95063, BF365255, T51687, BF332864, R74559, H83131, AW341133, BE549357, AW471002, BE762765, BE891260, H83132, AI356017, BE740064, BG011025, BF247697,

HTXFL30	599	620001	1 - 1977	15 - 1991	BE762774, H44274, AW086147, BE762767, BF923679, N98698, AV684676, R51880, AW898923, AI431971, BE548022, AI203034, AA766045, AI823509, AW071576, AW295813, R62584, AA028993, BE018806, AA765554, AA017568, N49971, H48233, BG006485, AI277213, R79503, BF591992, H78111, R62585, R22076, AI206462, N54046, AI752881, AI220633, BF857686, AA580842, BF592158, H05682, H67771, AI949890, AI675025, AW602075, C21303, AW384997, AI583730, AA317754, AK001484.1, AF151803.1, AL049839.3, AL353678. 11.
HTXKP95	600	891275	1 - 961	15 - 975	BE891940, BF851322, W28069, AW298651, AA112484, T08083, BF955273. AI934965, AW574868, BF056901, BE676636, AA831751, AA814605, AW590381, AI857985, AA742405, BF592924, AI697328, BF039191, AW450001, AI341301, AI635420, AW610280, AA917582, AI418901, C01813, BE694168, AW291415, AA751165, BF798709, BF916068, AW975618, AW966330, AV718489, AW964468, AV699866, C14331, AV718681, AV720791, AW966065, AV718931, AW966389, AV724520, AW949645, D80522, AV738340, AV699550, D80133, D59610, AW973541, AV718692, D81026, AW960465, AW975613, AW975605, D80248, AW965177, AW377671, C14429, AW964532, AV722801, D80251, AW949641, AV720731, AW973488, AW973445, D51060, D51799, AW959469, AV741191, AV718938, AV718633, AW949630, C14389, AW978634, AW966062, D51423, AV720203, D80366, AW959799, AV719324, AW966059, AW973490, D59859, AV701004, AW959582, D80166, AW973474, AW964756, AW966053, D59619, D80269, AW978661, D80210, AW960553, D80240, D80253, AV719822, AW973307, AW964477, AW956434, AW973447, AV699927, AW966369, AV718707, AV720211, AV720878, AV719557, D80241, AV699447, D50979, AW966029, AW958993, D81030, AV723927, AW959136, AW966075, AW949656, D59373, AW949642, D80188, AW959202, AV720035, AW973334, AW966531, AW966534, D80227, AW966333, D58283, AW966022, D80212, AW978648, AW960473, D50995, AW966013, D59467, D51022, D80022, AW966041, D80219, AV719188, D80195, AW975621, AW959628, AW966378, AW973485, AW965163, D80391, D80164, D59275, AW966030, AW966054, AW966050, AW965158, D80043, D59787, AW959062, AV718440, AV719783, AV720028, D59502, AW959597, AW959570, AV719468, AV718800, AW965185, AW965197, AW965196, AW965184, AW965175, AV718844, AV720464, AV718770, AW973330, AW973482, AW958992, AW964488, AW962082, AW949654, D57483, C15076, D59889, D59927, D80196, AV720151, AV720533, D80024, D80378, AW949657, AA305409, AW966386, AW960454, AW962395, AW966368, AV720616, AW966032, AW966331, AW966398, AW966397, AV701839, AW956397, AW949629, AW949653, AW949631, AW949643, AW949618, AW949655, AV720220, AW966399, AA305578, AA514188, AV744662, D80038, AW966385, AW966043, AV744012, AW960504, AW973473, D80193, AW966388, AW962245, AW966380, AW965176, AW964737, AW966400, AW966332, AW966053, AV741187, AV741198, AV721386, AW949646, AW949633, AW949632, AW949658, D80045, C14014, AV744004, AA514186, AV744690, AV702035, D80268, AW752082, AV700889, AW753053, AW177440, AW966023, AV742001, AV720812, AV723097, AW966377, AW975623, D80439, AV744006, D59627, AW360811, AW178893, AV718530, BC008360.1, AC008083.23, AC004242.1.

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HTXKP61	601	824083	1 - 1195	15 - 1209		BE275577, BF342801, AL529204, AL660428, AW003481, AL469418, BG231875, AU160542, AW003722, BE221902, AL530582, AI697903, BE741000, AU144726, AA433918, AI371156, AA029908, BF516011, AI017052, AI150233, AA846607, AI095354, AU118071, AL042959, AI653247, AI338204, AA552385, AL528110, AI001078, AI168113, W31264, AL529205, AW449063, BF510837, AI061060, AI251838, AW770273, AA810494, AW383853, AI582444, AW440361, AI337406, F25991, AA040569, AA030037, BG258196, R52694, R60246, R61272, AI225083, BE562335, AI474379, AA813625, BE503451, AW957171, T33316, F08876, AI394687, BF797612, AA706515, AI372806, BE407233, AA938133, AI962262, AA694463, AA806149, BG256771, AA371703, AL523910, BE384815, BF087775, H56115, AI265837, BG151348, BF930219, H05238, BE397686, AW840116, H18625, AW166747, AW839962, AI832256, BF793735, R46092, F09405, AI570516, AI832533, AI264936, AI201947, AI916913, AA076196, AI206207, BF813476, F08877, AI468489, AI949645, AI273819, AA732023, AA743249, AI918304, AA425605, BE047789, BF084883, BF374860, BG119332, N91827, Z40907, BE560246, AW008923, AI085806, BF003088, T65375, BF765564, BG230772, AA214506, BF843766, BE907797, AA868644, BF914189, AI372805, AA034314, T47081, BF685922, AW383854, AI493557, AA670130, AL036905, BF724094, BF882198, AW750565, AW816798, AW175913, BE727732, AA215302, AA436121, AA040668, AI424583, AA434601, R88938, BC002855.1, BC008053.1, AL136657.1, AL137200.1, AK021605.1, AB037846.1, AF265228.1, AL035417.15, AC005043.2.
HUDBZ89	602	135221 1	1 - 2121	15 - 2135		AU125474, BE883532, BG107414, BE898459, BE746984, BE542496, BF575571, AW958579, BF314540, BF573504, BE734208, AI802426, AW953779, AW292502, AU149129, BG031927, AA436628, AA076658, AU150986, BF081743, AA046746, BF095716, AA046670, BE186054, AW601449, AW673051, AW294732, AW601455, AI910194, BE092409, AI601235, H66950, H66951, R85537, AA363520, AI202299, R40736, AA363830, BF085875, AV749014, BE876022, AW190087, AL520949, AA808657, T98596, AW896216, T98595, AA355808, AW377204, AW377198, AA079565, AW377106, BE699057, AW377170, AW752839, AW362224, AI223245, BE832662, AW579894, AW579890, AI362898, AW377180, AB007866.2, AL109823.23.
HUFBY15	603	135234 9	1 - 1179	15 - 1193		AW389141, AW609901, BF374842, BF374845, AW388854, AW389152, BF374846, AW389148, AW389140, AW388908, BF374844, AW752215, AI797737, AW662557, AW375776, AW389144, AI990471, AA625286, AW388954, AW271542, AW752222, BF032067, AI953121, BE504740, AW389077, AW388858, AA303053, AI991077, AA303052, AW388926, AA613119, AA297581, AI963985, AW388918, AW388731, AW388732, AW388759, AA524545, BF513041, AW811008, AL132639.4.
HUFEF62	604	645101	1 - 504	15 - 518		BF929940, AU137259, BE065411, AU128307, AW818223, BE154234, BE065240, BE065404, AW856804, BE065281, BE065188, BF755156, AW939313, AW876637, BE065282, AW936927, BE065231, BE866484, BE065242, AU121120, AW992038, BF577152, BE612443, BE065370.

AV731147, BE161681, BE065317, AV732111, BE679479, BE065413, AW969925, AV730460, AW857254, BE065118, BF104734, BF759242, BE082759, AV709803, BF755153, AV730235, BF037518, AA977057, BF836355, AW876639, BF948215, AW996889, BF755154, AW935656, AW973139, AA528530, BF734987, AA191204, AL046030, AW855823, AU135945, AW501852, BF969464, AW863794, AW890245, BE139153, BE085108, AL119323, BE065280, AA601495, BE011046, AA493718, AL046784, BE011043, AL624655, BE011042, AW896115, AA761416, BE972565, AL120423, AW302839, BG010346, BF959938, R84363, BF960892, AA682353, AL042414, BF962824, AL041416, BF831226, T06958, AW993651, BF854999, BF956969, BF736812, BF962008, BF753245, BF772428, BF673759, BF916693, AW993753, BF883025, BF923362, AV730003, A1026925, BE157145, AV704579, T71060, R79525, BF893577, AA325164, BE064368, BE157315, AA205322, AA346163, AA457283, BF809496, BE011045, AA533484, AU137226, BF210705, BF895153, AL120163, AV732374, AW812457, BF751447, AL557245, AA554985, AV655163, AA321733, AV732067, BE206708, AV729982, BE044670, BF679337, AA113115, T06803, AA491346, AA219222, AW391396, BE011047, BF687597, BF964256, AA180025, AA577884, AW866346, BF930824, BE165031, AV731981, BE257366, AL298238, AW855161, AW937257, BE019645, T63711, BE007920, AL133996, BF920901, N20799, AA504676, AU135263, W03937, AA584718, AA996004, AW063432, BE074928, BE074925, BE074924, BE074927, BE074929, AA113109, AU122701, BE894098, AW818666, BE074926, D44828, BE074930, AA157151, AV730114, AA332197, AA181443, AA018677, AA601206, AA339620, AV732054, T57463, AW900157, N89024, AA322003, AW818530, AU137873, AV754121, AA457599, BE877368, AW892118, BF792872, AA745295, AA101399, AV730285, BF820471, BF753251, BF759243, AL139090.11, AL138680.15, AC020987.8, AC010146.13, AC005213.1, AF229557.1, AC019097.5, AC018676.5, AP001880.4, AC006399.6, AC009517.5, AC006313.1, AL132800.4, AP002364.3, AC011745.4, AL136090.12, AL021069.1, AL590084.9, AL360236.26, AC008471.6, AC010191.24, AC073655.26, AL353140.12, AC005188.1, AC069304.7, AP002534.1, AL512403.9, AP000532.1, AL132795.12, AC010395.6, AC012610.5, AL031054.1, AL031665.19, AL121939.12, AL132657.33, AC020941.5, AL355589.8, AC002429.1, AL390027.11, AL161443.13, AC002471.5, AC005374.5, AL035466.3, AL360219.18, AC020647.9, AC009404.5, AP000365.1, AC004385.1, AC005160.1, AL139115.5, AC007090.3, AC091491.1, AJ246003.1, AC079316.15, AC022416.5, AC002403.1, AP000548.1, AF194537.1, AC068139.5, AC016643.6, AC021269.4, AL512445.5, AP001883.5, AP001429.2, AL034351.1, AC024589.4, AC008162.3, AC004543.1, AL445209.4, AC005373.1, AC068722.6, Z85997.1, AC005823.1, AC067947.6, AL121947.14, AL121658.2, AC010632.6, AC068797.29, AL031585.1, Z95704.1, AB020874.1, AC005399.19, AP001978.4, AC011998.8, AL356100.8, AP001818.2, AL133320.8, AC002981.1, D83253.1, Z68871.1, AC004845.2, D87004.2, AC079468.3, AC022224.22, AF117829.1, AC012442.7, AL031393.1, AL135926.12, AC090945.1, AL360085.26, AL356801.5, Z84470.1, AC006350.2, AL391380.12, AP001860.2, AC008493.4, AC002432.1, AF190464.1, AC007380.3, AC004982.1, AC004550.3, AL109764.2, AC019212.4, AL158850.8, AC026167.4, AL590675.3,				
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HUKAH51	605	135242 4	1 - 839	15 - 853	AC010234.5, AL391416.9, AC005741.1, AL139812.11, AC011743.6, AC013290.4, AC010623.7, AC010679.6, AC023281.13, AC016968.24, Z94056.1, AC083861.2, AC055120.5, AC008463.6, AL034405.16, AC008664.5, AL158206.8, AL590043.7, AC007611.5, AL162373.16, AP001607.1, AC004864.1, AL096793.20, AC010499.5, AL139106.12, AC005993.2, Z97987.1, AJ006345.1, Z96074.4, AL035415.22, AC008430.3, AL512310.3, AC078843.2, AJ009615.3, AC002106.1, AL353753.6, AL049828.3, AP000797.5, AL096800.20, Z82205.1, AC021133.5, AL050309.4, AC004946.1, AC008782.6, AL049589.15, AL132673.17, AL117342.12, AL136970.8, AC018616.5, AC005603.1, AL359545.12, AC007402.3, AL079303.3, AL109941.17, AL109758.2, AC078851.4, AC007248.3, AL353764.9, AC008474.7, AP000547.1, AC008805.7, AL391065.6, AL136525.17, AP003471.2, AC016956.19, AC058784.17, AC069227.24, AL157775.15, AC020943.5, AC005740.1, AL031768.9, AP003467.2, AC078814.22, AL109845.8, AC006374.2, AC004885.2, AC025442.5, AC010528.8, AC005799.1, AF036235.1, AC025040.7, AC010368.4, AC005532.1, AL117351.12, AL080275.20, AC023480.6, AP002088.2, AC009318.11, AC076972.16, AC010145.9, AL133334.16, AC006357.5, AL163541.13, AL353691.12, AL160267.17, AL078638.9, AC007001.2, AL109761.3, AC009046.4, AC010651.7, AC003064.2, AC026161.4, AC003687.1, AF196972.1, AC006131.1, AL158093.8, AL162500.15, AL162719.18, AL355530.6, AC002416.1, AL034399.6, AC022367.34, AL031985.10, AC008243.6, AL158153.10, AL357045.10, AL079305.3, AC016651.6, AL162579.16, AC018503.6, AC004748.1, AL121927.24, AP000314.1, AC008716.6, AL109621.5, AL158147.17, AC007444.1, AL161916.8, AL008713.1, AL137017.9, AL390802.2, AL391420.16, AC005604.1, AC006061.1.
HUKBT29	606	694590	1 - 1743	15 - 1757	AA502331, AA503839, AW592433, AW444616, AW957011, AA568450, AI017393, T85589, T72043, T78178, AW079940, T85588, AI699382, AA299977, BF593574, T86494, AW605240, AW956056, AA335186, AA551860.
HUSIG64	607	566762	1 - 996	15 - 1010	AI889172, AI080136, AA211445, AA211523, F24617, AA211502, F27978, AW614056, AI862904, BG222837, F28119, F30666, F29048, AI972919, AA211549, AI128717, Z24989, AW302460, F28086, F26294, Z28706, AA413432, R45814, BG014944.
HUSXS50	608	135236 7	1 - 2547	15 - 2561	AUI132783, AUI13545, BE879986, BE875866, BE875592, AUI138137, AI343496, BE889561, BE179171, BF437308, AI627188, AW514639, AUI128177, AUI128176, AI287966, AA862577, AUI123709, AI674555, AUI138293, AA917000, AI811236, W52793, BF790472, AV746689, RS2090, AW241400, AA948155, AW964602, AI762045, AI971433, Z40332, R49159, AUI136203, R81617, BG024648, BE843297, AA969855, BE816922, BE769518, BE816921, BE816943, BE816951, AUI138770, T30870, BF329070, BE835821, BF671946, AUI138360, AUI135153, BE179399, BF982177, BE769579, BE816923, Z44401, Z24991, AW379766, R81358, BE819508, AW946464, AA383566, AW956753, AW946480, D86326.1, AK002093.1.

BF97657, BE869619, BE616370, BE616612, BF306220, BF306195, AV655974, AW978168, BF305460, BG120823, BE560047, AW978171, BE882111, BF037530, BE676498, BE251660, BE270241, BF203303, BE902628, BF309616, BE267578, BG033765, AA485950, BE065146, BG254407, BF310813, BE312978, BF306475, BE905968, BF446006, BF737387, AW984420, N22768, AA176598, AW984416, BF125825, AW984417, BF307029, H95262, AW984415, BF435055, BF979227, BE693917, BE732765, AW984418, AW984423, BF306361, AV753202, AV690488, AA176958, AW984338, AI751645, AI301138, AA315010, AI830086, AW984422, AA176601, BG057361, BE390359, BE314347, BF307951, BG120049, T66123, BF030495, BE348975, BE675980, BE905732, BE538385, R61430, AA176961, AW337133, AW189210, AI264229, BF727126, BF573743, BF979483, AA779980, AW984421, AI142549, BF305130, BE931839, BE297623, BF941393, AA451629, BE044637, AW984413, BF308011, AW192745, AW027544, W37275, AA827128, BG115366, AI151013, AA034495, AA604131, AV650977, AI127612, AW150320, AI524711, AW973257, AI861987, AI469431, AW090258, AI985865, AI129524, AI129524, H37844, AA063465, AA151284, AW513431, H99312, AW984346, AI312744, BF819503, AA781668, AA026636, AI093350, AI089601, N25147, BG235957, AA191371, H72514, AA115146, BE298404, AA309734, AV749302, AA127064, AA709104, AA779590, BE901613, AW075416, W94571, BF375767, AA429862, H96717, AI438596, AI751646, AA828465, W65488, AI144280, N70034, AA630583, BF379967, W94665, AI990143, AW074204, N54139, AI360050, AI139072, AI298031, N31021, BE246664, AA151285, AA113370, AI673233, AA279340, N55099, AA341830, AW984344, AA620847, BF928260, AI289617, AW074213, AW364601, N58667, AA777063, AA489561, AW887094, N95463, R81022, BG055405, AA766203, AI038290, AA025249, T58352, AW189287, AW028461, AI633400, AW984345, AI147792, AI299766, BF799616, H75310, AI200071, BE561076, BG249896, AI499250, AA354776, W65499, AA809914, AI903841, AI453808, T71499, H10629, H58855, AI094411, R87151, AW089182, W96032, H81218, H81223, AV726304, R95799, AI370222, AA548305, R66175, AA814999, W80425, H94290, AA216453, BF798979, AA927662, H81224, W25203, H66405, BF092277, W02774, N48499, BE278547, N40461, AA846361, H19408, AA602474, AV738327, R89366, BF448937, BC008361.1, AL050254.1, AF233225.1, AF129537.1, Z71183.2, AL021937.1, AL035068. 3.					
HVARW53	609	119481 2	1 - 1001	15 - 1015	AI991013, AW600302, BE045875.
HWAAD63	610	838626	1 - 3294	15 - 3308	BG058664, AW953071, BF668217, AL046409, AI284640, AW406162, BF852604, AU123691, AL046205, AW303196, D82290, AW301350, AI334443, AV761286, AL121235, AW274349, AW600804, BF339640, BF677892, AV763892, BG032943, AI572924, AI801482, AI431303, AL044940, AV740801, AV764490, BG249643, AV762098, AI270117, AW969629, AI732378, AW265385, AI963720, AI708009, AI350211, AU147104, AW473163, AA669840, AV735495, AI149478, AV763971, AA581903, AV759518, AV760937, AI754955, AL041690, AI583283, AV710066, AV763550, BG236735, AU145314, AW502975, AV742057, BG167743, BF940837.

HWABA81	611	580889	1 - 852	15 - 866	AP000045.1, AL136123.19, AC007011.1, AL357150.7, AC008753.8, AL121675.36, AC002551.1, AL157838.24, AC009516.19, AC004865.1, AL139230.25, AC005297.7, AL050335.32, AC007216.2, AL049759.10, AP001716.1, AL021546.1, AC000360.35, AP001718.1, AE006639.1, AC025436.2, AL359091.10, AC004940.1, AC008101.15, AC003029.2, AL352978.6, AC020983.7, AL118520.26, AC007272.3, AC005154.1, AC078878.20, AL136980.5, AC005778.1, AC004971.3, AL033383.26, AC005921.3, AL159995.8, AC008068.4, AL008718.23, U95742.1, AC068712.6, AL024474.1, AC005031.1, AC017091.8, AC090514.1, AP001666.1, AL158040.13, AL161799.19, AL133387.8, AC003108.1, AC005808.1, AL109825.23, AC004033.3, Z98051.6, AC005295.1, AL353764.9, AC011236.8, AL132768.15, AC006285.11, Z99716.4, AL139396.17, AL096840.25, AL022098.1, AC005052.2, AC002300.1, AC007066.4, AL109797.18, AC004686.1, AL031662.26, AC008812.7, AL161656.20, AL136961.19, AC007404.4, AC020550.4, AJ003147.1, AP001858.4, AC021203.5, AC011559.3, AL117258.4, AC007620.30, AC010553.6, AP002028.1, AL356575.8, AP000299.1, AL121748.6, AL136300.22, AC016257.22, AC003684.1, AC004941.2, AL157406.19, AL049694.9, AL162853.17, U66059.1, AC026464.6, AL121972.17, AC013264.4, AL162426.20, AC006345.4, AC090960.1, AL049742.7, AC005037.2, AP000359.1, AC007051.3, AC018633.2, AL133174.15, AC008474.7, AC018635.6, AB023049.1, AC034198.6, AC022211.5.
HWABA81	611	580889	1 - 852	15 - 866	BE676856, AL121897.32.
HWABY10	612	768334	1 - 2936	15 - 2950	BG110964, BF795642, BF338736, BF344299, BF339610, BF344724, BE905985, BG171717, BF663359, BE878057, BF344117, BF797494, BE779728, BG110428, BE548198, BG113392, BE514891, BG105728, BF344895, BF342409, BE731592, BF344700, BF326253, BG107408, BF337274, AA029404, BE873119, BF339289, BE537567, BE546615, BF215522, BF348090, BF341943, BF974666, BG106809, AW517110, BE866817, BF337936, BE312135, BF342571, BF339613, BF795397, BE259965, BG025377, AW328067, AW051360, BF112053, AW467352, AW328066, BF305147, BF432273, BF925893, AW517104, AI921698, AI683501, BF338943, BE910326, AW732485, BF338023, BE465948, W38916, AA779337, BF854480, BE045837, W25986, AA973853, AA101157, AW084136, AA181835, AA775283, AA186569, W68073, AI560223, AI147239, AI089340, AI095449, BE670405, AA082143, AI066562, AA679092, AI422300, AI613463, AA588711, BG176783, AI761003, AI088731, AW051882, AI126290, BE646503, AA837279, AW087365, AI148227, AA009501, AI283584, AI434557, W28104, T62574, AI951073, AA782618, AI479881, W47512, N46795, AI985937, N40931, AI039397, AI432803, AI583386, BF802889, BF832903, BF804217, AW956881, W46793, BF802896, W68195, BG230721, BF815862, BG222416, BG222489, AI083847, BF806737, N40938, AI684916, AW576132, BF805055, W45117, W27429, AA324201, BF876216, AA862278, AI627377, Z43491, W26072, BF871297, W46921, AW518033, BG055999, AA071418, BF339697, BF432684, BF664265, H87824, BF804896, AI369040, N46788, AI280551, AW393985, BF343179, AI961956, R54302, AW393954, AA021161, W25922, AA574349, BF819220, BF933082, T08587, AI954952, T03895, AA910718, BF832997, BF833048, R60251, AI272774, AI682434, AW351625, AI369469, BF432394, W47511, AA366238, AA021160, AW394010.

					<p>BF814966, BF089042, BF155712, AA379745, AA877680, BF834816, BF359736, BF155722, AI373184, BF833953, N79680, AI370695, AI633094, AI244521, AW367090, BF832989, AI564952, T60257, Z39561, BF832028, BF964430, AA071417, BF831958, AI475015, AA843970, BF834819, BF831774, BF832084, BF128611, BF838597, AW243364, BF832026, R51913, AW973898, BF834823, AA381066, BE868310, AA077947, BF832092, F34684, AA318041, F03657, T63198, BF834818, N62740, AW407707, AI905924, AA844604, AA594549, BF834825, AA036914, BF749722, AI962077, T03318, T30346, AW902956, BE874414, T61397, AI915039, AI097627, BF831259, BE829374, BF832901, BF941457, H87774, BF094249, AW243479, BE563198, AW003146, BF752515, AW589814, BE815641, AW518327, BE714416, AA782804, BF831773, BF155715, AA026160, AA628683, AL136610.1, AK000539.1, AC073347.3, AC073237.3, AL162008.1, AF126488.1, BC008784.1, AL359932.1, BC004905.1, AL157480.1, BC006480.1, BC008282.1, AK026541.1, BC004119.1, BC008488.1, AL122049.1, AF218031.1.</p>
HWADJ89	613	799506	1 - 1755	15 - 1769	<p>AW958273, AW377130, AW574767, AW138853, BF111962, AA135712, AA156931, AW264402, AW117200, AI684896, AW339989, AA524553, AI394626, AI754796, AI860485, AI989549, AW129957, AI672796, BG056354, AA040909, AI000898, AI421190, AI693729, AW512733, AW044450, AI090274, AW205364, AW081734, BE939287, N35410, AA788655, N55117, AA844145, AI091868, N62863, AW302517, AI361489, AI628038, AA765992, AI800010, AI817849, BF800164, AI285397, AW403436, AA658416, AA648845, F13408, N73777, AA983941, R34886, AI024148, T04873, AA310563, Z33435, R72500, AI219780, AI149773, BG248348, R49268, BE305119, BE293618, AI743430, AW440724, T78828, BE249965, F10993, BE250024, AI371489, BE171979, N77769, AW235832, AI204426, R34492, N48042, BF899137, BF842700, R34372, Z38685, N99398, AI857456, AW841803, BE176205, AW899803, AA665233, AI290874, AW591407, AI432644, BF757092, AI623302, AW968355, AI431347, AI432653, AW081103, AI431230, AI431328, AI432654, AI432655, AI431310, AI431312, AI432650, AI432677, AW968356, BE672759, AI431353, AW971740, AW972091, AW972093, AW968729, AI431307, AI431316, AI432661, AI431354, AI431315, AI431337, AI431257, AI492519, BE672745, BE672732, AI791349, AI432666, AI432675, AW128900, BE672748, AI431238, AI492520, BE672719, AI432651, AI432647, AI431330, AI432674, AI432672, BF448552, AW972092, BE672767, AI431243, AI431248, AI432665, AI432657, AI432658, AI432649, BE672644, AI431255, BE672774, BE672742, AW969229, AI431254, BF589777, AI431350, AI431231, AI432662, AI431345, BE672738, AI431357, AW858522, AI431241, AI431351, AI431323, AI431346, AI431247, AI431318, AI432676, AI432673, AI431235, AI431321, AW128897, AI431340, AI432643, BE672792, AW128846, AI432664, AI431246, AW972090, AI432645, AW128884, BE672743, AI492510, BE672640, AL042931, AI431314, AW129223, AI431308, BE672749, BE672744, AI492509, BE672622, AI431751, BE672627, AL042729, AL045494, AL042655, BE672626, AL042523, AL042519, AL042853, AL031296.1, AK026719.1, AB007922.2, AF052104.1, AF064854.1, AL133082.1.</p>
HWBAO62	614	838164	1 - 1889	15 - 1903	<p>AI683471, AI792952.</p>

HWBAR88	615	836469	1 - 1037	15 - 1051	AV704722, BF890753, BE832379, AA334103, BF513764, AI654920, AW418882, BE503701, AI949038, AI093540, AA703125, AI076049, AI356640, AI359681, AI160128, BE858525, AV717717, AI422536, AB020316.1, AL357992.14, AL590485.7, AL359252. 17.
HWBCB89	616	109334 7	1 - 1303	15 - 1317	BE383506, AW957082, BF965615, AA749209, BE314194, BE856755, AW959644, AA406605, BF673639, AI635816, AI332841, AW576111, AI925364, AA599283, BE646653, AA815259, AI093865, AA557291, AA992639, AI199140, AI094047, AA778372, AA777994, BF110030, AA700564, AW236389, AW405247, AI376136, AW195935, AA418750, AA418959, AA809375, AI378198, W47086, AA258421, AA833614, AA722806, AW135736, AI312116, N26019, AI401448, BE047114, AI004747, N36650, AA297567, AA975019, AA369324, F32728, AW592186, AA298693, AA248246, AA214511, AA298744, AA248186, R01364, AA651996, AI382499, AA215364, AW241153, AW167882, AI038732, AL514627, AL514919, AV681857, AL513907, AA421957, AV756703, AL514473, AL513597, AL514791, AV682351, AL567360, AL135661, AI679916, AV756477, AL513803, AW087445, AV726951, BF904180, AL514691, BF792469, AV682330, BF726603, AV710479, AV706777, AV682266, BE965432, BE966388, AV758179, BG105099, BG257535, BE879906, AI499381, AW162071, AV717725, BG179993, BG112879, BF681080, BE964614, AI349772, AV682222, AL514155, AV757598, AL120854, BG036846, BF969484, BF971016, AV755207, AA640779, AV729334, AI633419, AI282903, AW301409, AI569616, AI433976, BF925729, AV682249, AV755581, BE963035, BG110517, BG109270, BG120816, BF343241, AI537677, BF970449, AW827289, BF883916, AL514935, BF724691, BE965481, BG122481, AL079963, AW103371, BG110684, AL513763, AI799199, AL036802, BF812933, AI868831, AV723953, BE048071, AI857296, BF904258, BF882343, BF795712, AV721967, AI678357, AL119863, AI521012, BF055737, BE964812, BG260037, AI498579, AV756360, AL045500, AW071349, BG105078, AW088899, BF344652, BF054789, BE964700, BG168696, AL048871, AI696626, AW068845, AI612913, AI572418, AI783792, AW238730, N80094, AI802240, BG180996, BG256950, AV757455, AL040243, AV681668, AI610645, AW983783, AI250663, BE876038, AI538085, AI620287, BF970162, AI702433, AL119791, AL045903, AI567351, AI280661, BE621256, AI537617, BF342070, AV682792, AI872914, BF034349, BG027082, BG108324, AA572758, AL036146, AV733824, AV681987, AV757096, AV758806, AI538716, AV755613, BF694790, AW268253, AI591316, BF726160, AI636456, AV682326, BF981774, AI121328, AI312428, AI281779, AI584140, BF673434, BG031815, AI950664, AV729890, AI680498, AV686346, AI682743, AW071417, BF792961, AI349004, BE881155, AV714975, BE966443, AI648663, AW148320, AI340582, BG250190, AI500077, AI349645, AV682051, AW149236, AI224992, AI289937, AI906328, AV716613, AV699193, AI564719, AI922676, BF343172, AW074993, AI349614, BG032208, BE781369, BE172767, BF793644, AK027683.1, AF091092.1, AL133640.1, S78214.1, AK025339.1, AF078844.1, AK000137.1, AB060908.1, AB049758.1, BC008387.1, AF090943.1, AF090934.1, AB063008.1, AF177336.1, AL512718.1, AF125949.1, AL512733.1, AL050393.1, AF090901.1, AL157431.1, AL133016.1, AL133606.1, AF104032.1, AF090900.1, AK000614.1, AL049938.1,

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HWBCP79	617	846382	1 - 1124	15 - 1138	

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HWBDP28	618	135226 5	1 - 1827	15 - 1841	BE889490, AV722484, BF939302, BF925193, BF675397, BF925185, AI885403, BF894252, BF437150, BF511298, BF925900, AI970784, AI669189, AW402243, AI635202, AI669779, AI241438, AW571832, AI473658, AW291412, BF925180, AA374925, AI612948, BF925863, BE885616, AK026147.1, M73469. 1.
HWBFE57	619	907063	1 - 1119	15 - 1133	BF893888, BE247495, BF756575, AF328787.1, AF250238.1, AF140342. 1.
HWDAC39	620	131081 7	1 - 739	15 - 753	AI685116, AW827247, AA446110, AL038713, AW838167, AI627336, AI377100, AI635355, AV652234, AW962432, AI610326, BE158597, BF949364, BF764903, AW102963, BF438919, BE973780, AI186380, AI220812, AI193408, AI873822, AV740374, AI598077, AI382347, BE873986, AI572522, AI926394, AI092624, AV744706, AI245554, AI053905, AI559986, BE048806, AI805962, BF092872, AW090566, AI758697, AL157902.6, AC007390.3, AC017082.4, AC013604.9, AC083875.1, AC002385.1, AL157938.22, AC005209.1, AL135938.9, AC017006.4, AC006198.1, AL031736.16, AL133370.4, AL390057.12, AC078958.30, AC009405.3, AL359292.12, AL136164.8, AL158192.15, AL138703.10, AC004848.1, AC007877.3, AC010590.7, AC008739.5, AL445433.14, AL353707.14, AL158015.9, AL079304.3, AL121857.5, AC025436.2, AC011361.4, AC020915.6, AL354736.10, AC021188.6, Z82161.1, AC016398.5, AL391811.7, AL162853.17, AL356019.5, AC008059.2, AL392087.7, AC061958.11, AL121841.5, AL591291.1, AC016720.9, AC016770.10, AC027239.5, AL365227.19, AC012003.9, AL139090.11, AC007482.7, AL034561.5, AL355305.9, AC025445.4, AL161665.5, AL109852.13, AL078614.2, AL390838.26, AL160273.9, AL356115.9, AL391379.12, Z98749.11, Z93018.1, AP002534.1, AL161617.17, AI271735.1, AL035246.13, AC025613.14.

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HWD4H38	621	102851 9	1 - 1590	15 - 1604	AA410788, AU147162, AW069227, AW805539, AU278089, AW578373, BF769368, AW054995, AF1733856, AI890324, AW849032, AI923052, AA547979, AU144540, AI634187, AI056177, AA847499, BF681619, AW861303, AW500029, AA916430, AV762633, AI457313, AA228778, BG250286, AI732389, AI754653, BE138594, BF675251, AI537020, AW973992, AA158190, AI679002, AW168433, AI891080, AW514662, AL079734, BE062159, AA515728, AA491423, BF832074, AA832145, BE897079, AW674631, AW798093, BF725178, AI049630, AW068596, AA579179, BG115297, AW004884, AW084445, AI923050, AW575000, AI282479, AU152561, AL120282, BF917346, AW338035, AW338021, AL038842, AA719073, AV762009, T09219, AW971987, AW338179, AA669155, AA502991, BG222875, AI279417, AA491955, AA236867, AA640710, AW872575, AI254770, AA223174, BE042511, AI821714, AI791913, AV756491, AI284126, AI792133, AI821785, BE139139, AI251034, AA176604, AW302315, AA569648, BG236628, AV759518, AA714110, AI133164, AC008481.7, AE006639.1, AC006057.5, AL049776.3, AC004846.2, AL035404.20, AC008397.7, AL355593.21, AC002544.1, AL031311.1, AL590762.1, AC002045.1, AJ400877.1, AP001051.1, AC004882.2, AC004840.3, AC008623.4, AP000046.1, AF129756.1, AC007021.3, AL136526.27, AL133367.4, AC007957.36, AL513131.1, AC008569.6, AC008687.4, AL137077.31, AL359252.17, AC010543.8, AC007216.2, AC016601.6, AC011449.6, Z83844.5, AF038458.1, AC008891.7, Z83845.14, AC007686.5, AL050318.13, AC011500.7, AC004024.2, AL022323.7, AC002073.1, AC019184.3, AL359236.4, AF288742.1, Z95115.1, AC003667.1, AL445222.9, AC008280.4, AL353802.14, AC010616.5, AC009131.6, AC004531.1, AP001721.1, AL358777.12, AL139317.5, AC005037.2, AL031666.6, AC002553.1, AL359092.14, AL163300.2, AL162426.20, AL163249.2, AF047825.1, AL079335.29, AC005015.2, U95740.1, AL133163.2, AL121586.31, AC004228.2, AC005049.2, AC004867.5, AL118520.26, AL391833.10, AC002365.1, AP000356.1, AC00517.2, AL590763.1, AC008395.6, AL139415.10, AL031717.11, AL354864.16, AC009996.7, AP001718.1, AC008543.7, AL354735.14, AC005079.6, AF243527.1, AC080012.20, AC005280.3, AL033518.14, AL354760.11, AL035406.25, AC040160.4, AC034193.4, AL356915.19, AC079177.21, AC005488.2, AC020917.4, AC008812.7, AC018663.3, AC005052.2, AP001724.1, AC005972.1, AC051619.7, AC006441.13, AC008074.3, AC010422.7, AC006285.11.

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HWHG71	622	995431	1 - 1007	15 - 1021	AA927633, BE206519, H85594, AA019612, BF379185, BF829931, AF308571.1, AB008193.1, AF277230.1, AB029892.1, AJ278605.1, AF190901.1, D89079.1, U41070.1.
HWHG49	623	135225 7	1 - 971	15 - 985	BE907577, AU126910, AL533833, BE731437, AW970004, BF967077, BE788909, BF207957, BF343694, BE737688, BE866037, BE272694, BF208159, H1761, BE564507, R52799, BF965044, BF208977, BF676791, N94214, AV657236, BF725860, N91665, AA588382, BF725223, H70673, BF813629, R17380, R22829, BE772590, H55988, BE962738, BF210281, BF889390, BF208466, C04806, N80329, D56451, AF797289, H59335, BF879857, AW008969, AI394269, BE795342, D56220, BE740614, BE793846, BF732877, AI541453, R01796, BE903639, BE790851, BF880011, Z36872, AW582547, BE267419, BE742662, BF026122, BE735825, BE793469, BF949650, AW885466, AW009897, BG170115, AA248589, AW062936, AI148761, AI928801, AW858815, BE903214, BF689981, AW178925, T69554, AI278793, BE513607, AW363731, BE730258, BE393241, BE727175, AW263105, H93411, R62171, AA613553, N30347, BF125876, AA960959, BE265249, AA996071, AW818608, BF184855, AI026967, BF026858, AW069303, AA148228, BE958392, AA193652, AW577228, AA235201, BE887401, AW247577, H41429, BE799132, BF967713, BF243020, AA837473, AW247732, AI917109, R86909, BF211115, AV716597, T34155, AW577215, C05230, AA316485, AI751446, AI276480, AI750270, BE798194, BE934366, BE934317, BE934437, BE934332, AA316485, AI751446, AI276480, AI750270, BE798194, BE934366, BE934317, BE934437, BE934332.

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HWHGUS4	624	695695	1 - 1431	15 - 1445	AA458648, BE140448, AA455546, AL132708.3, AL132990.3.
HWHGZ51	625	886212	1 - 1685	15 - 1699	BE735965, AW372956, BF826018, BE735558, AW007721, AI955624, N30735, BF842481, AA531286, BE735650, AA476961, AA479609, AA709157, N29329, BF813297, AI680020, BF814081, W72299, AW450151, BF349121, AI342682, BE713111, AI207356, BE713103, BE713065, AA459897, AI206356, W23589, BF349122, BE939515, BE714549, W76325, W35267, AW272943, AA158001, AA442947, BE713172, BG012569, T69460, AA321599, AW135072, AA369339, BE713162, AI202455, AA369441, N57021, W68131, BE713086, BE713074, T69437, BE713165, AI301772, T70492, T70513, BF738317, AW389438, BE717812, D29356, BE717821, AA127911, AA846442, AA127966, BF842499, BF739402, BE140441, BE048026, AV658585, AL037582, AL037602, BG179993, AI802542, AV741327, AI628337, BE184331, N29277, AL040241, AW079572, BF812960, BF792961, AV743962, BG114432, AI469505, AL042745, AV757865, AI079963, BF970768, AI698391, BG110684, AI499285, BE968711, BF751302, AI570807, AI345416, AI345612, BF726183, AI824576, BF724420, AI345415, BE789764, F37323, AI627988, BG256090, AL043355, BG113188, BF856052, AV658845, AI884318, AI491775, AV656595, BF924855, AI886594, BG104927, AW051088, BF032768, BG111560, AV713305, BF526020, AI540458, AA287231, AW880037, AV733448, AI288285, AW983832, BF725534, BE047852, BG029086, BF970652, AA580663, BE963838, BG167986, AI538850, AI580436, AW673679, BF055899, AI440239, AI685005, AI687295, BG058150, AA833760, AA225339, AI241923, AI568138, BE018334, BG033723, BF054877, BG115626, BF338002, AL042744, AW303152, BG001235, AI673363, BG030364, AW090393, AI783997, AL042191, BF812938, BF752245, BF727091, AI670009, AV718258, AW020561, AI433157, AI818358, AI702073, AI473536, BF911521, AV757052, BF868489, AV682124, AI682798, T95813, BF812961, AI570966, AL036214, AI345778, AI932794, AW163834, BE879108, AW827206, AI564259, BG110682, BG058398, AA641818, AI633125, AI866040, BE535384, AI538564, AI638798, AW161156, AI915291, AW152182, BG117375, AW051059, BF811804, AV681993, BG166654, AI866770, AL041150, AW104141, AI800440, BE877904, BF086116, AI433590, BE069120, AA806720, BE778453, BG180605, AL036673, BG112456, AI969655, AV733734, AL514887, AW827103, BG028116, BE964614, AI539847, AI863191, AI254727, AL039086, AI445992, BF885081, AI345608, BG029667, AI345688, AW083573, AI572717, AL036631, BF816037, AI613038, AW834302, BF909758, AW026882, AL038445, AI868931, R36271, BF872365, BG110517, BG257547, BG164558, AI267454, AI581033, AI623941, AI568114, AW167918, AA743354, AV714798, AV757035, AW983829, BF794478, AI223603.2, AF082889.1, AC018758.2, AL353940.1, BC006472.1, AF132676.1, AF061836.1, AL137533.1, AL137294.1, AB055352.1, AF262032.1, AL137271.1, AL137480.1, AF056191.1, AL117435.1, AL080154.1, X72889.1, AK024538.1, BC004370.1, AB047941.1, AL389935.1, AL117460.1, BC002473.1, AL136845.1, BC006103.1, AL389939.1.

					AB050431.1, Z82022.1, AL512733.1, BC003548.1, AL122093.1, AB052191.1, AK026762.1, AL110221.1, AL049430.1, AL359583.1, AF217982.1, AF146568.1, AL050155.1, AB062750.1, AL137476.1, AL137557.1, AB060873.1, BC001655.1, X65873.1, AL512718.1, AB055371.1, AL137463.1, AB056427.1, AK027144.1, BC008282.1, AL442082.1, AK026600.1, AL133606.1, AF285167.1, AL122050.1, AB050410.1, AK026642.1, BC004925.1, AK025414.1, AB060908.1, AK025435.1, BC007534.1, AL136864.1, AL137488.1, AL080148.1, AL512719.1, AL512750.1, AK026480.1, BC003614.1, AL390154.1, BC004530.1, AB056421.1, BC007053.1, AK026593.1, AK024594.1, X82434.1, AK000418.1, AB047904.1, AB060929.1, AK027146.1, AL133665.1, AF104032.1, BC005007.1, BC008673.1, AB060826.1, AK026583.1, BC009395.1, AL135956.1, AB049758.1, AL137658.1, AL080137.1, AF100781.1, AF090934.1, AF358829.1, AL137478.1, AB055370.1, BC004899.1, AK026613.1, BC000090.1, AK026506.1, BC002733.1, AF321617.1, AB062978.1, AL137479.1, S61953.1, BC005858.1, AF218031.1, AK026885.1, BC002523.1, BC000348.1, AF061795.1, AF151685.1, AY034001.1, AK026542.1, AF320073.1, AF026816.2, AK024992.1, AK027081.1, AJ299431.1, AK026626.1, BC008417.1, AL137550.1, AK025491.1, AL359601.1, AL117578.1, AL136893.1, AL359618.1, U80742.1, AF111112.1, BC008387.1, AK027096.1, AL133640.1, AF225424.1, AL137459.1, AF183393.1, BC004958.1, AB048975.1, AB063079.1, AB056809.1, AB052200.1, AK026927.1, AF061943.1, AL096744.1, AF090901.1, AF057300.1, AF057299.1, X98834.1, AL133067.1, Y16645.1, AL133558.1, AK026528.1, AB063070.1, AK027161.1, BC006440.1, AF177336.1, AL136844.1, AB056420.1, AL137538.1, AB063093.1, AK027164.1, AL136843.1, BC007567.1, AL133075.1, AK025312.1, AF125948.1, AL583915.1, AL157431.1, AK025484.1, BC008078.1, BC008893.1, AK025465.1, AL137548.1, AL137521.1, AL136784.1, AL050366.1, AK027868.1, AF230496.1, AK026855.1, AB060905.1, AB060837.1, AL096720.1, AK026462.1, AL136540.1, BC004349.1, X69819.1, BC004951.1, BC004362.1, BC009212.1, Y14314.1, AL050149.1, AL110225.1, AL122098.1, AL136892.1, AL389982.1, AL136805.1, AL050277.1, AK026504.1, AK025391.1, AK027121.1, AB048953.1, AC021325.5, AL512754.1, AB063074.1, AK026630.1, AL080234.1, AL162062.1, AL359620.1, AB063100.1, BC001844.1, AB055361.1, AK024570.1, BC008983.1, AL359941.1, AB060912.1, BC003683.1, AB060897.1, AF143723.1, BC005168.1, AK026744.1, AL117416.1, BC004195.1, AK026784.1, AL122100.1, AL122118.1, AB056768.1, AY033593.1, BC007499.1, AL110280.1, AL133560.1, AL080124.1, AK026647.1, BC009033.1, AK024588.1, AK026086.1, AL049283.1, BC008899.1, AB048919.1, AK026959.1, AK000647.1, AB048974.1, AL136792.1, Z37987.1, AL137529.1, BC007680.1, BC006525.1, BC001056.1, AL050116.1, BC003684.1, AL137558.1.
HWHHL34	626	805642	1 - 1515	15 - 1529	AL529775, AL533489, AL524594, BF974297, AL516570, BG163363, BE881103, AL146476, BG120063, BE259554, BF342974, AV715318, BE789938, BG105343, AV755514, BE780157, BF691658, AW812911, BG024181, AW812981, BF213502, AV716562, BF698515, BG261045, BF574514, BF211692, BF033068, BF348164, AV759171, AV701423, BF035763, AW955608, AW812971, AW581981, BF677888, BF571378, BF576293, BF240656, AW390493, BE222633,

HWLEV32	627	103260 2	1 - 1204	15 - 1218	<p>BF690640, BF576363, AW813018, BF699331, AV714362, BF978687, BE866124, BF672111, BF674211, BF670420, BE866568, AV755701, AI814859, BF665931, N92494, AI829932, BF698791, BF031127, W02193, BF671702, BF982689, BF184136, BF673226, W52978, AV681672, AI523284, AV753993, BF104739, AI192376, AW581987, AW390508, BF692915, AW367258, BF693474, BF977859, AA714791, BF036599, BF575352, BF671401, BE967567, BF242452, AV712182, BE891500, BF216657, BF681132, BF791182, AV716096, BE873981, AV733846, AW444946, BF031577, BE042514, BF215151, BF670720, BF573310, AW338919, AV712127, AV755085, AW369344, BE568177, BF213846, C05938, AL524593, BF243276, BF031685, BE973611, BF671286, AA309028, AW367331, BG258889, BF248358, BF693807, C14373, BF673387, BF666055, AI570372, BF970299, BF694056, AI886726, BF693641, AV751806, BF697207, C17464, AV759457, AI934573, BF214152, AA071179, BF819215, BF840385, BF131605, AI142543, BF575523, BF573716, BF574652, AA143582, BF106013, AI124903, AW162310, BF676442, BE855418, AA608786, BF239036, D59738, AL119812, BE874284, BF032570, AA430087, AW160345, BE961116, BF241468, BF843268, BF240051, AA977077, W16602, AA835662, AA080889, AA278398, BE568227, AW516026, AI066530, AA069864, AA569765, AI143310, AA665803, AI360862, AI277781, AI374863, AI138742, BG010683, BF693336, BE439719, BF988814, AA074132, AI376131, AV756060, BF675761, AI031953, AI953405, BF000793, AA928916, BE939314, AV755293, BF208002, AA446457, AA453448, BF575432, AA036868, AA904672, T93097, BE565473, AI684677, D59612, AV717305, AI167882, BF836349, AI300824, BF246928, R83429, AA583427, D80223, BF432205, R78724, BF671408, AA187223, BE549552, AW016459, AA009661, AI267156, AI687932, BF998029, AW609216, W58390, R83437, AI091900, AA846357, BE866710, AV648956, AI075421, AI752663, AV744633, AV734138, AW401449, BF196720, AA078834, BF571477, AI032001, BF369911, AI057310, AW149028, AW836319, D80244, AI077911, AI143583, AA309029, BF382245, AI640870, AI934317, AA810465, BF239551, AA835669, C18148, N20411, BE866744, BF243507, AA932432, N44506, AA083615, AA724827, AA612714, AA775846, AF125530.1, BC005143.1, AF070523.1, AF064854.1, T92495, T93191, T86811, T97284, T97396, R39633, R82460, H00317, H00365, H03492, H03590, H25943, H25977, H44243, H44581, R83332, R83338, H78436, N34780, N74004, W02766, W24795, W39502, AA069875, AA078872, AA084246, AA186346, AA426275.</p> <p>AA677440, AW994068, AA368613, AW052024, AI633325, AA865554, AA011059, AA011060, AW955888, AU156208, BE177677, AF198488.1, AL137740. 1.</p> <p>AW663887, AA702920, AI042498, BF981980, AA661749, AW401902, AI286001, AW237708, AA512902, AW503623, BE645601, AW405179, AW973049, Z39825, AA129086, AL134524, AW972845, AW975037, AW979204, AW975032, AW976024, AW979127, AW972292, AW975002, AW975965, AW975628, AW970942, AW861944, AW969988, AW971403, AW979098, AW975105, AW858525, AW975019, AW972849, AW025744, AW974801, AW971404, AW975954, AW877209, AW975031, AW969791, AW979002, AW974786, AI088353, AW973219, AW972867, AW979238, AL119324, AW971375, AW979212, AW970540, AW979090, AW979176, AW975154, AW979294,</p>
HWLIH65	628	793713	1 - 817	15 - 831	<p>AW663887, AA702920, AI042498, BF981980, AA661749, AW401902, AI286001, AW237708, AA512902, AW503623, BE645601, AW405179, AW973049, Z39825, AA129086, AL134524, AW972845, AW975037, AW979204, AW975032, AW976024, AW979127, AW972292, AW975002, AW975965, AW975628, AW970942, AW861944, AW969988, AW971403, AW979098, AW975105, AW858525, AW975019, AW972849, AW025744, AW974801, AW971404, AW975954, AW877209, AW975031, AW969791, AW979002, AW974786, AI088353, AW973219, AW972867, AW979238, AL119324, AW971375, AW979212, AW970540, AW979090, AW979176, AW975154, AW979294,</p>

					<p>AW970079, AW973397, AW969673, AW971968, AW973717, AW976023, AW975971, AW969885, AW975876, AW975952, AW975649, AW969643, AW975020, AW975254, AW975025, AW975650, AW969680, AW974964, AW979106, AW858522, AW975981, AW846262, AW975942, AW970070, AW975028, AW968181, AW975027, AW975990, AW975434, AW970969, AW975966, AW975632, AW972680, AW976511, AW968212, AW974823, AW974975, AW969839, AW974338, AW973750, AW969816, AW974658, AW972296, AW971732, AW979169, AW969852, AW976000, AW976031, AW974785, AW969793, AW972721, AW979220, AW971975, AW969911, AW979219, AW970936, AW975230, AW975596, AW969637, AW975015, AW858455, AW968347, AW976982, AW979173, AW972880, AW972817, AW969748, AW975244, AW970050, AW975930, AW969861, AW975585, AW979147, AW973819, AW979142, AW974101, AW858526, AW970101, AW972154, AW968207, AW968204, AW451860, AW975022, AW971378, AW979232, AW970889, AW973214, AW975959, AW973254, AW972649, AW979133, AW979113, AW973785, AA456016, AW973654, AW969785, AW979208, AW970927, AW979211, AW974802, AW971326, AW971305, AW970107, AW976506, AW975626, AW970010, AW970113, AW976035, AW975231, AW975149, AW975084, AW972884, AW970025, AW972695, AW973805, AW972719, AW976515, AW969633, AW975921, AW969921, AW975157, AW979165, AW979054, AW971254, AW976510, AW971954, AW975941, AW974089, AW973230, AW975975, AW969778, AW969884, AW974962, AW972943, AW969759, AW979083, AW970587, AW979175, AW979037, AW973986, AW979064, AW975938, AW975016, AW970921, AW969766, AW979116, AW972806, AW973987, AW972706, AW973164, AW973824, AW970097, AW974393, AW970094, AW971964, AW975904, AW974379, AW969752, AW973718, AW973967, AW975933, AW973734, AW973207, AW972882, AW973104, AW969782, AW970868, AW972868, AW973985, AW975648, AW973821, AW971129, AW969930, AW972864, AW979178, AW969658, AW972883, AW979081, AW972933, AW975162, AW971183, AW971387, AW970110, AW972705, AW972827, AW973946, AW976012, AW972823, AW970589, AW971259, AW971350, AW975261, AW971367, BC008596.1, AK001798.1, AL122101.1, AL133053.1, AL136763.1, AL133049.1, AL133074.1, AL136755.1, AL136758.1, AL133076.1, AL136764.1, AL136762.1, D17247.1, AL133082.1, AJ276251.1, AJ276253.1, AJ276255.1, AJ276256.1, AL133068.1, AB026436.1, AL136825.1, AJ276254.1, AL133655.1, AF141306.1, AL133020.1, AF002985.1, AF126531.1, Z69719.1, AE006462. 1.</p>
HWTBK81	629	460568	1 - 623	15 - 637	<p>T89795, AW769449, AA774621, AA954176, BF879355, H04799, BF879528, BE394321, R39277, T89429, R42299, AA873122, AC009238.4, AC008268.3, AC016683. 7.</p>
HYAAJ71	630	826754	1 - 3323	15 - 3337	<p>AV718385, AV718481, AV659465, AV659453, AV659577, AV659377, BF894682, AV704375, AI284640, AA581903, AL046205, AW576391, AW265385, AI334443, BG249643, AW265393, AW301350, AW270270, AW303196, AW502975, AI307201, AL046409, AI345654, AL042853, BG171422, AF330238, AI076616, AA533333, AI538852, BF680041, AA526787, AL037683, AI355206, AV738303, AV710066, AA584082, BF679304, AA491284, AI270117, AW419262, AW103758, AA468022, BF677892, BF816072, AI431303, AV730952, BG109996, AW274349,</p>

BF918590, AI469968, AI537506, AW274346, BG107801, AW193265, AI368256, BF991286, AV658688, AV652936, AI963720, BF678911, AI120687, AA584201, AA490183, BF683672, AW438643, AV658733, AI281881, BF592200, AA126450, AI042420, AW872676, AW731867, AI148277, AA468131, BF813686, BF592311, AV740801, AW020992, AV763550, BF676981, BF914859, AV762009, AA610491, AI613280, AW473163, AW072587, AV710770, AV762959, AW162489, AW270382, BF724372, AI375542, AV761631, AV702857, AA521323, BF679274, AU148742, BE049095, AI358571, AI956131, BF725315, AW500353, AA584167, AW088718, AW872575, AI610376, AA629572, AI041690, BE967369, AV764398, AW970848, AA720702, AU145393, BF919090, AV757607, AI287651, AA613345, BF984160, AI432270, AI890918, AV759172, AF074677, AV739901, BF680639, AV764530, AW975425, AI718446, AW129001, BF697673, AV733830, AA528725, AV728425, AV764241, AW833862, BF056371, BF792603, BF347791, AW969629, BF347740, F36306, AW979031, AA602047, AA491831, AI583283, BE139146, BG036337, AI568678, AW407578, AW472872, AV760937, BF965007, AI379719, AW265009, AI350211, AU147800, AA722372, BF679107, AI064952, AI085719, AV763354, BF942454, AV762395, AA079348, AV704536, AA491814, AV725423, AV761155, BE206443, AA577959, BF841869, AI539563, AU154961, AI034405.16, AC006353.3, AC069262.24, AC004987.2, AL121972.17, AC026866.8, AC007371.16, AI136170.12, AC002395.1, AP000719.4, AL121601.13, AL1356915.19, AP000140.1, AL136992.22, Z86061.1, AC068724.7, AC020916.7, AC008753.8, AF038458.1, AC009530.5, AC022384.4, AC008403.6, AL022238.1, AC005304.1, AC006989.3, AC068712.6, AL354763.17, AC010422.7, AC005548.1, AC007564.9, AC091492.1, AC018769.2, AP000088.1, AC004826.3, AP000228.1, L78833.1, AP000459.3, AC002126.1, AC003957.1, AP001718.1, AC008519.4, AC008249.14, AL133284.13, AC008946.6, AP002797.3, AL157838.24, AL009179.1, AL117381.32, AC011455.6, AC013737.4, AL096841.6, D84394.1, AP000508.1, AL157882.5, AL122035.6, AC012379.7, AL049759.10, AL136300.22, AC007384.3, AC006501.5, Z99128.1, AC008064.2, AC013429.12, AC006211.1, AC067722.21, AL137802.7, AL163973.1, AC002544.1, AC000066.1, AC004840.3, AC004453.1, AL354935.23, AC018696.4, AC024082.6, AC023114.5, AC007919.18, AL031904.1, AC019046.4, AC008812.7, AC023511.17, AC006285.1.1, AL391137.11, AL022323.7, AP001667.1, AP001714.1, AP001687.1, U67229.1, AP001972.4, AC008101.15, AC005291.1, AL163249.2, AL033378.12, AC005539.1, AP001694.1, AC002430.1, AC005358.1, AC007620.30, AC034193.4, U63313.1, AC004751.1, AP003357.2, AL356244.12, AL121899.37, AC022432.4, AC006006.2, AC009179.17, AC007318.4, AJ010770.1, AC027319.5, AL354720.14, AL135839.15, AF109907.1, Z82244.1, AL157938.22, AL139039.17, AL021453.1, AC012003.9, AC011484.4, AC002565.1, AL021154.1, AJ010598.1, AL161656.20, AP001717.1, AC018507.3, AL161742.7, AL355516.12, AC087071.2, AL158194.16, AL391807.13, AP000345.1, AL049869.6, AC004992.1, U91326.1, AC018808.4, AC022383.3, AC004547.1, AL450104.14, AC010102.3, AC010679.6, AL139385.12, AL365232.24, Z95152.1, AF196779.1, AC005907.1, AC010650.8, AP000755.4, AC004534.1, Z95116.1, AC005911.6, AL358214.10, AC007193.1,					
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					AP001835.4, AC005252.1, AC004008.1, AL133551.13, AC009947.2, AL096862.18, AC016027.15, AC006435.7, AC090952.2, AC020893.5, AC027458.4, AL132780.5, AP000517.1, AC006597.2, AL133279.7, AC019233.7, AC006040.3, AC005859.1, AC007272.3, AL135924.11, D83989.1, AC005914.1, AL121900.26, AC016697.8, AL022476.2, AC003101.1, AL135752.6, AL139809.16, AL031286.1, AC007324.55, AC006448.14, AL161799.19, AC008891.7, AC011497.6, AL138885.21, AL365475.1, AL357034.18, AC005412.6, Z69917.1, AC016830.5, AP001700.1, AL136338.4, AC073492.18, AC005393.1, AL035411.27, AC007561.4, AL354932.26, AL080242.11, AC020901.8, AC034198.6, AC004686.1, AL139021.6, AP000959.2, AL138726.12, AC004166.12, AC007014.1, AL353807.18, AL035659.22, AL049692.13, AC016601.6, AC005189.1, AL391833.10, AC005209.1, AC078878.20, AL450265.11, AC004678.1, AC011286.7, AC005940.3, AL162853.17, AC018719.4, AC084865.2, AP001716.1, AC004019.20, AL023280.1, AF200465.1, AL023807.6, AL359835.10, AC005375.4, AL451075.15, AC004213.1, AL136358.13, AC005694.3, AC026391.6, AC023473.3, AL356094.11, AC009144.5, AC015801.25, AL162426.20, AC005900.1, AC078846.2, AE006462.1, AL359236.4, AL356481.16, AC016894.7, AL355497.14, AL136969.7, AL359265.8, AP003466.2, AL008715. 1.

Description of Table 4

Table 4 provides a key to the tissue/cell source identifier code disclosed in Table 1B.2, column 5. Column 1 of Table 4 provides the tissue/cell source identifier code disclosed in Table 1B.2, Column 5. Columns 2-5 provide a description of the tissue or cell source. Note that "Description" and "Tissue" sources (i.e. columns 2 and 3) having the prefix "a_" indicates organs, tissues, or cells derived from "adult" sources. Codes corresponding to diseased tissues are indicated in column 6 with the word "disease." The use of the word "disease" in column 6 is non-limiting. The tissue or cell source may be specific (e.g. a neoplasm), or may be disease-associated (e.g., a tissue sample from a normal portion of a diseased organ). Furthermore, tissues and/or cells lacking the "disease" designation may still be derived from sources directly or indirectly involved in a disease state or disorder, and therefore may have a further utility in that disease state or disorder. In numerous cases where the tissue/cell source is a library, column 7 identifies the vector used to generate the library.

Table 4

Code	Description	Tissue	Organ	Cell Line	Disease	Vector
AR022	a_Heart	a_Heart				
AR023	a_Liver	a_Liver				
AR024	a_mammary gland	a_mammary gland				
AR025	a_Prostate	a_Prostate				
AR026	a_small intestine	a_small intestine				
AR027	a_Stomach	a_Stomach				
AR028	Blood B cells	Blood B cells				
AR029	Blood B cells activated	Blood B cells activated				
AR030	Blood B cells resting	Blood B cells resting				
AR031	Blood T cells activated	Blood T cells activated				
AR032	Blood T cells resting	Blood T cells resting				
AR033	brain	brain				
AR034	breast	breast				
AR035	breast cancer	breast cancer				
AR036	Cell Line CAOV3	Cell Line CAOV3				
AR037	cell line PA-1	cell line PA-1				
AR038	cell line transformed	cell line transformed				
AR039	colon	colon				
AR040	colon (9808co65R)	colon (9808co65R)				
AR041	colon (9809co15)	colon (9809co15)				
AR042	colon cancer	colon cancer				
AR043	colon cancer (9808co64R)	colon cancer (9808co64R)				
AR044	colon cancer 9809co14	colon cancer 9809co14				
AR050	Donor II B Cells 24hrs	Donor II B Cells 24hrs				
AR051	Donor II B Cells 72hrs	Donor II B Cells 72hrs				
AR052	Donor II B-Cells 24 hrs.	Donor II B-Cells 24 hrs.				
AR053	Donor II B-Cells 72hrs	Donor II B-Cells 72hrs				

AR054	Donor II Resting B Cells	Donor II Resting B Cells							
AR055	Heart	Heart							
AR056	Human Lung (clonotech)	Human Lung (clonotech)							
AR057	Human Mammary (clonotech)	Human Mammary (clonotech)							
AR058	Human Thymus (clonotech)	Human Thymus (clonotech)							
AR059	Jurkat (unstimulated)	Jurkat (unstimulated)							
AR060	Kidney	Kidney							
AR061	Liver	Liver							
AR062	Liver (Clonotech)	Liver (Clonotech)							
AR063	Lymphocytes chronic lymphocytic leukaemia	Lymphocytes chronic lymphocytic leukaemia							
AR064	Lymphocytes diffuse large B cell lymphoma	Lymphocytes diffuse large B cell lymphoma							
AR065	Lymphocytes follicular lymphoma	Lymphocytes follicular lymphoma							
AR066	normal breast	normal breast							
AR067	Normal Ovarian (4004901)	Normal Ovarian (4004901)							
AR068	Normal Ovary 9508G045	Normal Ovary 9508G045							
AR069	Normal Ovary 9701G208	Normal Ovary 9701G208							
AR070	Normal Ovary 9806G005	Normal Ovary 9806G005							
AR071	Ovarian Cancer	Ovarian Cancer							
AR072	Ovarian Cancer (9702G001)	Ovarian Cancer (9702G001)							
AR073	Ovarian Cancer (9707G029)	Ovarian Cancer (9707G029)							
AR074	Ovarian Cancer (9804G011)	Ovarian Cancer (9804G011)							
AR075	Ovarian Cancer (9806G019)	Ovarian Cancer (9806G019)							
AR076	Ovarian Cancer	Ovarian Cancer							

	(9807G017)	(9807G017)							
AR077	Ovarian Cancer (9809G001)	Ovarian Cancer (9809G001)							
AR078	ovarian cancer 15799	ovarian cancer 15799							
AR079	Ovarian Cancer 17717AID	Ovarian Cancer 17717AID							
AR080	Ovarian Cancer 4004664B1	Ovarian Cancer 4004664B1							
AR081	Ovarian Cancer 4005315A1	Ovarian Cancer 4005315A1							
AR082	ovarian cancer 94127303	ovarian cancer 94127303							
AR083	Ovarian Cancer 96069304	Ovarian Cancer 96069304							
AR084	Ovarian Cancer 9707G029	Ovarian Cancer 9707G029							
AR085	Ovarian Cancer 9807G045	Ovarian Cancer 9807G045							
AR086	ovarian cancer 9809G001	ovarian cancer 9809G001							
AR087	Ovarian Cancer 9905C032RC	Ovarian Cancer 9905C032RC							
AR088	Ovarian cancer 9907 C00 3rd	Ovarian cancer 9907 C00 3rd							
AR089	Prostate	Prostate							
AR090	Prostate (clonotech)	Prostate (clonotech)							
AR091	prostate cancer	prostate cancer							
AR092	prostate cancer #15176	prostate cancer #15176							
AR093	prostate cancer #15509	prostate cancer #15509							
AR094	prostate cancer #15673	prostate cancer #15673							
AR095	Small Intestine (Clontech)	Small Intestine (Clontech)							
AR096	Spleen	Spleen							
AR097	Thymus T cells activated	Thymus T cells activated							

AR098	Thymus T cells resting	Thymus T cells resting					
AR099	Tonsil	Tonsil					
AR100	Tonsil germinal center centroblast	Tonsil germinal center centroblast					
AR101	Tonsil germinal center B cell	Tonsil germinal center B cell					
AR102	Tonsil lymph node	Tonsil lymph node					
AR103	Tonsil memory B cell	Tonsil memory B cell					
AR104	Whole Brain	Whole Brain					
AR105	Xenograft ES-2	Xenograft ES-2					
AR106	Xenograft SW626	Xenograft SW626					
AR119	001: IL-2	001: IL-2					
AR120	001: IL-2.1	001: IL-2.1					
AR121	001: IL-2_b	001: IL-2_b					
AR124	002: Monocytes untreated (1hr)	002: Monocytes untreated (1hr)					
AR125	002: Monocytes untreated (5hrs)	002: Monocytes untreated (5hrs)					
AR126	002: Control.1C	002: Control.1C					
AR127	002: IL2.1C	002: IL2.1C					
AR130	003: Placebo-treated Rat Lacrimal Gland	003: Placebo-treated Rat Lacrimal Gland					
AR131	003: Placebo-treated Rat Submandibular Gland	003: Placebo-treated Rat Submandibular Gland					
AR135	004: Monocytes untreated (5hrs)	004: Monocytes untreated (5hrs)					
AR136	004: Monocytes untreated 1hr	004: Monocytes untreated 1hr					
AR139	005: Placebo (48hrs)	005: Placebo (48hrs)					
AR140	006: pC4 (24hrs)	006: pC4 (24hrs)					
AR141	006: pC4 (48hrs)	006: pC4 (48hrs)					
AR152	007: PHA(1hr)	007: PHA(1hr)					

AR153	007: PHA(6HRS)	007: PHA(6HRS)							
AR154	007: PMA(6hrs)	007: PMA(6hrs)							
AR155	008: 1449_#2	008: 1449_#2							
AR161	01: A - max 24	01: A - max 24							
AR162	01: A - max 26	01: A - max 26							
AR163	01: A - max 30	01: A - max 30							
AR164	01: B - max 24	01: B - max 24							
AR165	01: B - max 26	01: B - max 26							
AR166	01: B - max 30	01: B - max 30							
AR167	1449 Sample	1449 Sample							
AR168	3T3P10 1.0uM insulin	3T3P10 1.0uM insulin							
AR169	3T3P10 10nM Insulin	3T3P10 10nM Insulin							
AR170	3T3P10 10uM insulin	3T3P10 10uM insulin							
AR171	3T3P10 No Insulin	3T3P10 No Insulin							
AR172	3T3P4	3T3P4							
AR173	Adipose (41892)	Adipose (41892)							
AR174	Adipose Diabetic (41611)	Adipose Diabetic (41611)							
AR175	Adipose Diabetic (41661)	Adipose Diabetic (41661)							
AR176	Adipose Diabetic (41689)	Adipose Diabetic (41689)							
AR177	Adipose Diabetic (41706)	Adipose Diabetic (41706)							
AR178	Adipose Diabetic (42352)	Adipose Diabetic (42352)							
AR179	Adipose Diabetic (42366)	Adipose Diabetic (42366)							
AR180	Adipose Diabetic (42452)	Adipose Diabetic (42452)							
AR181	Adipose Diabetic (42491)	Adipose Diabetic (42491)							

AR182	Adipose Normal (41843)	Adipose Normal (41843)							
AR183	Adipose Normal (41893)	Adipose Normal (41893)							
AR184	Adipose Normal (42452)	Adipose Normal (42452)							
AR185	Adrenal Gland	Adrenal Gland							
AR186	Adrenal Gland + Whole Brain	Adrenal Gland + Whole Brain							
AR187	B7(1hr)+ (inverted)	B7(1hr)+ (inverted)							
AR188	Breast (18275A2B)	Breast (18275A2B)							
AR189	Breast (4004199)	Breast (4004199)							
AR190	Breast (4004399)	Breast (4004399)							
AR191	Breast (4004943B7)	Breast (4004943B7)							
AR192	Breast (4005570B1)	Breast (4005570B1)							
AR193	Breast Cancer (4004127A30)	Breast Cancer (4004127A30)							
AR194	Breast Cancer (400443A21)	Breast Cancer (400443A21)							
AR195	Breast Cancer (4004643A2)	Breast Cancer (4004643A2)							
AR196	Breast Cancer (4004710A7)	Breast Cancer (4004710A7)							
AR197	Breast Cancer (4004943A21)	Breast Cancer (4004943A21)							
AR198	Breast Cancer (400553A2)	Breast Cancer (400553A2)							
AR199	Breast Cancer (9805C046R)	Breast Cancer (9805C046R)							
AR200	Breast Cancer (9806C012R)	Breast Cancer (9806C012R)							
AR201	Breast Cancer (ODQ 45913)	Breast Cancer (ODQ 45913)							
AR202	Breast Cancer (ODQ45913)	Breast Cancer (ODQ45913)							
AR203	Breast Cancer	Breast Cancer							

	(ODQ4591B)	(ODQ4591B)						
AR204	Colon Cancer (15663)	Colon Cancer (15663)						
AR205	Colon Cancer (4005144A4)	Colon Cancer (4005144A4)						
AR206	Colon Cancer (4005413A4)	Colon Cancer (4005413A4)						
AR207	Colon Cancer (4005570B1)	Colon Cancer (4005570B1)						
AR208	Control RNA #1	Control RNA #1						
AR209	Control RNA #2	Control RNA #2						
AR210	Cultured Preadipocyte (blue)	Cultured Preadipocyte (blue)						
AR211	Cultured Preadipocyte (Red)	Cultured Preadipocyte (Red)						
AR212	Donor II B-Cells 24hrs	Donor II B-Cells 24hrs						
AR213	Donor II Resting B-Cells	Donor II Resting B-Cells						
AR214	H114EP12 10nM Insulin	H114EP12 10nM Insulin						
AR215	H114EP12 (10nM insulin)	H114EP12 (10nM insulin)						
AR216	H114EP12 (2.6ug/ul)	H114EP12 (2.6ug/ul)						
AR217	H114EP12 (3.6ug/ul)	H114EP12 (3.6ug/ul)						
AR218	HUVEC #1	HUVEC #1						
AR219	HUVEC #2	HUVEC #2						
AR221	L6 undiff.	L6 undiff.						
AR222	L6 Undifferentiated	L6 Undifferentiated						
AR223	L6P8 + 10nM Insulin	L6P8 + 10nM Insulin						
AR224	L6P8 + HS	L6P8 + HS						
AR225	L6P8 10nM Insulin	L6P8 10nM Insulin						
AR226	Liver (00-06-A007B)	Liver (00-06-A007B)						
AR227	Liver (96-02-A075)	Liver (96-02-A075)						
AR228	Liver (96-03-A144)	Liver (96-03-A144)						
AR229	Liver (96-04-A138)	Liver (96-04-A138)						

AR230	Liver (97-10-A074B)	Liver (97-10-A074B)							
AR231	Liver (98-09-A242A)	Liver (98-09-A242A)							
AR232	Liver Diabetic (1042)	Liver Diabetic (1042)							
AR233	Liver Diabetic (41616)	Liver Diabetic (41616)							
AR234	Liver Diabetic (41955)	Liver Diabetic (41955)							
AR235	Liver Diabetic (42352R)	Liver Diabetic (42352R)							
AR236	Liver Diabetic (42366)	Liver Diabetic (42366)							
AR237	Liver Diabetic (42483)	Liver Diabetic (42483)							
AR238	Liver Diabetic (42491)	Liver Diabetic (42491)							
AR239	Liver Diabetic (99-09-A281A)	Liver Diabetic (99-09-A281A)							
AR240	Lung	Lung							
AR241	Lung (27270)	Lung (27270)							
AR242	Lung (2727Q)	Lung (2727Q)							
AR243	Lung Cancer (4005116A1)	Lung Cancer (4005116A1)							
AR244	Lung Cancer (4005121A5)	Lung Cancer (4005121A5)							
AR245	Lung Cancer (4005121A5))	Lung Cancer (4005121A5))							
AR246	Lung Cancer (4005340A4)	Lung Cancer (4005340A4)							
AR247	Mammary Gland	Mammary Gland							
AR248	Monocyte (CT)	Monocyte (CT)							
AR249	Monocyte (OCT)	Monocyte (OCT)							
AR250	Monocytes (CT)	Monocytes (CT)							
AR251	Monocytes (INFG 18 hr)	Monocytes (INFG 18 hr)							
AR252	Monocytes (INFG 18hr)	Monocytes (INFG 18hr)							
AR253	Monocytes (INFG 8-11)	Monocytes (INFG 8-11)							
AR254	Monocytes (O CT)	Monocytes (O CT)							
AR255	Muscle (91-01-A105)	Muscle (91-01-A105)							
AR256	Muscle (92-04-A059)	Muscle (92-04-A059)							

AR257	Muscle (97-11-A056d)	Muscle (97-11-A056d)						
AR258	Muscle (99-06-A210A)	Muscle (99-06-A210A)						
AR259	Muscle (99-07-A203B)	Muscle (99-07-A203B)						
AR260	Muscle (99-7-A203B)	Muscle (99-7-A203B)						
AR261	Muscle Diabetic (42352R)	Muscle Diabetic (42352R)						
AR262	Muscle Diabetic (42366)	Muscle Diabetic (42366)						
AR263	NK-19 Control	NK-19 Control						
AR264	NK-19 IL Treated 72hrs	NK-19 IL Treated 72hrs						
AR265	NK-19 UK Treated 72 hrs.	NK-19 UK Treated 72 hrs.						
AR266	Omentum Normal (94-08-B009)	Omentum Normal (94-08-B009)						
AR267	Omentum Normal (97-01-A039A)	Omentum Normal (97-01-A039A)						
AR268	Omentum Normal (97-04-A114C)	Omentum Normal (97-04-A114C)						
AR269	Omentum Normal (97-06-A117C)	Omentum Normal (97-06-A117C)						
AR270	Omentum Normal (97-09-B004C)	Omentum Normal (97-09-B004C)						
AR271	Ovarian Cancer (17717AID)	Ovarian Cancer (17717AID)						
AR272	Ovarian Cancer (9905C023RC)	Ovarian Cancer (9905C023RC)						
AR273	Ovarian Cancer (9905C032RC)	Ovarian Cancer (9905C032RC)						
AR274	Ovary (9508G045)	Ovary (9508G045)						
AR275	Ovary (9701G208)	Ovary (9701G208)						
AR276	Ovary 9806G005	Ovary 9806G005						
AR277	Pancreas	Pancreas						
AR278	Placebo	Placebo						
AR279	rIL2 Control	rIL2 Control						

AR280	RSS288L		RSS288L						
AR281	RSS288LC		RSS288LC						
AR282	Salivary Gland		Salivary Gland						
AR283	Skeletal Muscle		Skeletal Muscle						
AR284	Skeletal Muscle (91-01-A105)		Skeletal Muscle (91-01-A105)						
AR285	Skeletal Muscle (42180)		Skeletal Muscle (42180)						
AR286	Skeletal Muscle (42386)		Skeletal Muscle (42386)						
AR287	Skeletal Muscle (42461)		Skeletal Muscle (42461)						
AR288	Skeletal Muscle (91-01-A105)		Skeletal Muscle (91-01-A105)						
AR289	Skeletal Muscle (92-04-A059)		Skeletal Muscle (92-04-A059)						
AR290	Skeletal Muscle (96-08-A171)		Skeletal Muscle (96-08-A171)						
AR291	Skeletal Muscle (97-07-A190A)		Skeletal Muscle (97-07-A190A)						
AR292	Skeletal Muscle Diabetic (42352)		Skeletal Muscle Diabetic (42352)						
AR293	Skeletal Muscle Diabetic (42366)		Skeletal Muscle Diabetic (42366)						
AR294	Skeletal Muscle Diabetic (42395)		Skeletal Muscle Diabetic (42395)						
AR295	Skeletal Muscle Diabetic (42483)		Skeletal Muscle Diabetic (42483)						
AR296	Skeletal Muscle Diabetic (42491)		Skeletal Muscle Diabetic (42491)						
AR297	Skeletal Muscle Diabetic 42352		Skeletal Muscle Diabetic 42352						
AR298	Skeletal Muscle (42461)		Skeletal Muscle (42461)						
AR299	Small Intestine		Small Intestine						
AR300	Stomach		Stomach						
AR301	T-Cell + HDPBQ71.fc		T-Cell + HDPBQ71.fc						

	1449 16hrs	1449 16hrs					
AR302	T-Cell + HDPBQ71.fc 1449 6hrs	T-Cell + HDPBQ71.fc 1449 6hrs					
AR303	T-Cell + IL2 16hrs	T-Cell + IL2 16hrs					
AR304	T-Cell + IL2 6hrs	T-Cell + IL2 6hrs					
AR306	T-Cell Untreated 16hrs	T-Cell Untreated 16hrs					
AR307	T-Cell Untreated 6hrs	T-Cell Untreated 6hrs					
AR308	T-Cells 24 hours	T-Cells 24 hours					
AR309	T-Cells 24 hrs	T-Cells 24 hrs					
AR310	T-Cells 24 hrs.	T-Cells 24 hrs.					
AR311	T-Cells 24hrs	T-Cells 24hrs					
AR312	T-Cells 4 days	T-Cells 4 days					
AR313	Thymus	Thymus					
AR314	TRE	TRE					
AR315	TREC	TREC					
AR317	B lymphocyte,	B lymphocyte,					
AR318	(non-T; non-B)	(non-T; non-B)					
AR326	001 - 293 RNA (Vector Control)	001 - 293 RNA (Vector Control)					
AR327	001: Control	001: Control					
AR328	001: Control.1	001: Control.1					
AR355	Acute Lymphocyte Leukemia	Acute Lymphocyte Leukemia					
AR356	AML Patient #11	AML Patient #11					
AR357	AML Patient #2	AML Patient #2					
AR358	AML Patient #2 SGAH	AML Patient #2 SGAH					
AR359	AML Patient#2	AML Patient#2					
AR360	Aorta	Aorta					
AR361	B Cell	B Cell					
AR362	B lymphoblast	B lymphoblast					
AR363	B lymphocyte	B lymphocyte					
AR364	B lymphocytes	B lymphocytes					

AR365	B-cell	B-cell							
AR366	B-Cells	B-Cells							
AR367	B-Lymphoblast	B-Lymphoblast							
AR368	B-Lymphocytes	B-Lymphocytes							
AR369	Bladder	Bladder							
AR370	Bone Marrow	Bone Marrow							
AR371	Bronchial Epithelial Cell	Bronchial Epithelial Cell							
AR372	Bronchial Epithelial Cells	Bronchial Epithelial Cells							
AR373	Caco-2A	Caco-2A							
AR374	Caco-2B	Caco-2B							
AR375	Caco-2C	Caco-2C							
AR376	Cardiac #1	Cardiac #1							
AR377	Cardiac #2	Cardiac #2							
AR378	Chest Muscle	Chest Muscle							
AR381	Dendritic Cell	Dendritic Cell							
AR382	Dendritic cells	Dendritic cells							
AR383	E.coli	E.coli							
AR384	Epithelial Cells	Epithelial Cells							
AR385	Esophagus	Esophagus							
AR386	FPPS	FPPS							
AR387	FPPSC	FPPSC							
AR388	HepG2 Cell Line	HepG2 Cell Line							
AR389	HepG2 Cell line Buffer 1 hr.	HepG2 Cell line Buffer 1 hr.							
AR390	HepG2 Cell line Buffer 06 hr	HepG2 Cell line Buffer 06 hr							
AR391	HepG2 Cell line Buffer 24 hr.	HepG2 Cell line Buffer 24 hr.							
AR392	HepG2 Cell line Insulin 01 hr.	HepG2 Cell line Insulin 01 hr.							
AR393	HepG2 Cell line Insulin	HepG2 Cell line Insulin 06							

	06 hr.	hr.							
AR394	HepG2 Cell line Insulin 24 hr.	HepG2 Cell line Insulin 24 hr.							
AR398	HMC-1	HMC-1							
AR399	HMCS	HMCS							
AR400	HMSC	HMSC							
AR401	HUVEC #3	HUVEC #3							
AR402	HUVEC #4	HUVEC #4							
AR404	KIDNEY NORMAL	KIDNEY NORMAL							
AR405	KIDNEY TUMOR	KIDNEY TUMOR							
AR406	KIDNEY TUMOR								
AR407	Lymph Node	Lymph Node							
AR408	Macrophage	Macrophage							
AR409	Megakarioblast	Megakarioblast							
AR410	Monocyte	Monocyte							
AR411	Monocytes	Monocytes							
AR412	Myocardium	Myocardium							
AR413	Myocardium #3	Myocardium #3							
AR414	Myocardium #4	Myocardium #4							
AR415	Myocardium #5	Myocardium #5							
AR416	NK	NK							
AR417	NK cell	NK cell							
AR418	NK cells	NK cells							
AR419	NKYa	NKYa							
AR420	NKYa019	NKYa019							
AR421	Ovary	Ovary							
AR422	Patient #11	Patient #11							
AR423	Peripheral blood	Peripheral blood							
AR424	Primary Adipocytes	Primary Adipocytes							
AR425	Promyeloblast	Promyeloblast							

AR427	RSSWT	RSSWT							
AR428	RSSWTC	RSSWTC							
AR429	SW 480(G1)	SW 480(G1)							
AR430	SW 480(G2)	SW 480(G2)							
AR431	SW 480(G3)	SW 480(G3)							
AR432	SW 480(G4)	SW 480(G4)							
AR433	SW 480(G5)	SW 480(G5)							
AR434	T Lymphoblast	T Lymphoblast							
AR435	T Lymphocyte	T Lymphocyte							
AR436	T-Cell	T-Cell							
AR438	T-Cell,	T-Cell,							
AR439	T-Cells	T-Cells							
AR440	T-lymphoblast	T-lymphoblast							
AR441	Th 1	Th 1							
AR442	Th 2	Th 2							
AR443	Th1	Th1							
AR444	Th2	Th2							
H0002	Human Adult Heart	Human Adult Heart			Heart				Uni-ZAP XR
H0004	Human Adult Spleen	Human Adult Spleen			Spleen				Uni-ZAP XR
H0007	Human Cerebellum	Human Cerebellum			Brain				Uni-ZAP XR
H0008	Whole 6 Week Old Embryo								Uni-ZAP XR
H0009	Human Fetal Brain								Uni-ZAP XR
H0011	Human Fetal Kidney	Human Fetal Kidney			Kidney				Uni-ZAP XR
H0012	Human Fetal Kidney	Human Fetal Kidney			Kidney				Uni-ZAP XR
H0013	Human 8 Week Whole Embryo	Human 8 Week Old Embryo			Embryo				Uni-ZAP XR
H0014	Human Gall Bladder	Human Gall Bladder			Gall Bladder				Uni-ZAP XR
H0015	Human Gall Bladder, fraction II	Human Gall Bladder			Gall Bladder				Uni-ZAP XR
H0016	Human Greater Omentum	Human Greater Omentum			peritoneum				Uni-ZAP XR

H0017	Human Greater Omentum	Human Greater Omentum	peritoneum		Uni-ZAP XR
H0020	Human Hippocampus	Human Hippocampus	Brain		Uni-ZAP XR
H0022	Jurkat Cells	Jurkat T-Cell Line			Lambda ZAP II
H0023	Human Fetal Lung				Uni-ZAP XR
H0024	Human Fetal Lung III	Human Fetal Lung	Lung		Uni-ZAP XR
H0025	Human Adult Lymph Node	Human Adult Lymph Node	Lymph Node		Lambda ZAP II
H0026	Namalwa Cells	Namalwa B-Cell Line, EBV immortalized			Lambda ZAP II
H0030	Human Placenta				Uni-ZAP XR
H0031	Human Placenta	Human Placenta	Placenta		Uni-ZAP XR
H0032	Human Prostate	Human Prostate	Prostate		Uni-ZAP XR
H0033	Human Pituitary	Human Pituitary			Uni-ZAP XR
H0036	Human Adult Small Intestine	Human Adult Small Intestine	Small Int.		Uni-ZAP XR
H0038	Human Testes	Human Testes	Testis		Uni-ZAP XR
H0039	Human Pancreas Tumor	Human Pancreas Tumor	Pancreas	disease	Uni-ZAP XR
H0040	Human Testes Tumor	Human Testes Tumor	Testis	disease	Uni-ZAP XR
H0041	Human Fetal Bone	Human Fetal Bone	Bone		Uni-ZAP XR
H0042	Human Adult Pulmonary	Human Adult Pulmonary	Lung		Uni-ZAP XR
H0044	Human Cornea	Human Cornea	eye		Uni-ZAP XR
H0045	Human Esophagus, Cancer	Human Esophagus, cancer	Esophagus	disease	Uni-ZAP XR
H0046	Human Endometrial Tumor	Human Endometrial Tumor	Uterus	disease	Uni-ZAP XR
H0047	Human Fetal Liver	Human Fetal Liver	Liver		Uni-ZAP XR
H0048	Human Pineal Gland	Human Pineal Gland			Uni-ZAP XR
H0050	Human Fetal Heart	Human Fetal Heart	Heart		Uni-ZAP XR
H0051	Human Hippocampus	Human Hippocampus	Brain		Uni-ZAP XR
H0052	Human Cerebellum	Human Cerebellum	Brain		Uni-ZAP XR
H0056	Human Umbilical Vein,	Human Umbilical Vein	Umbilical vein		Uni-ZAP XR

	Endo. remake	Endothelial Cells				
H0057	Human Fetal Spleen					Uni-ZAP XR
H0058	Human Thymus Tumor	Human Thymus Tumor	Thymus		disease	Lambda ZAP II
H0059	Human Uterine Cancer	Human Uterine Cancer	Uterus		disease	Lambda ZAP II
H0060	Human Macrophage	Human Macrophage	Blood	Cell Line		pBluescript
H0061	Human Macrophage	Human Macrophage	Blood	Cell Line		pBluescript
H0063	Human Thymus	Human Thymus	Thymus			Uni-ZAP XR
H0065	Human Esophagus, Normal	Human Esophagus, normal	Esophagus			Uni-ZAP XR
H0068	Human Skin Tumor	Human Skin Tumor	Skin		disease	Uni-ZAP XR
H0069	Human Activated T-Cells	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0070	Human Pancreas	Human Pancreas	Pancreas			Uni-ZAP XR
H0071	Human Infant Adrenal Gland	Human Infant Adrenal Gland	Adrenal gland			Uni-ZAP XR
H0075	Human Activated T-Cells (II)	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0076	Human Membrane Bound Polysomes	Human Membrane Bound Polysomes	Blood	Cell Line		Uni-ZAP XR
H0078	Human Lung Cancer	Human Lung Cancer	Lung		disease	Lambda ZAP II
H0081	Human Fetal Epithelium (Skin)	Human Fetal Skin	Skin			Uni-ZAP XR
H0083	HUMAN JURKAT MEMBRANE BOUND POLYSOMES	Jurkat Cells				Uni-ZAP XR
H0085	Human Colon	Human Colon				Lambda ZAP II
H0086	Human epithelioid sarcoma	Epithelioid Sarcoma, muscle	Sk Muscle		disease	Uni-ZAP XR
H0087	Human Thymus	Human Thymus				pBluescript
H0090	Human T-Cell Lymphoma	T-Cell Lymphoma	T-Cell		disease	Uni-ZAP XR
H0097	Human Adult Heart, subtracted	Human Adult Heart	Heart			pBluescript

H0098	Human Adult Liver, subtracted	Human Adult Liver	Liver			Uni-ZAP XR
H0099	Human Lung Cancer, subtracted	Human Lung Cancer	Lung			pBluescript
H0100	Human Whole Six Week Old Embryo	Human Whole Six Week Old Embryo	Embryo			Uni-ZAP XR
H0102	Human Whole 6 Week Old Embryo (II), subt	Human Whole Six Week Old Embryo	Embryo			pBluescript
H0103	Human Fetal Brain, subtracted	Human Fetal Brain	Brain			Uni-ZAP XR
H0107	Human Infant Adrenal Gland, subtracted	Human Infant Adrenal Gland	Adrenal gland			pBluescript
H0108	Human Adult Lymph Node, subtracted	Human Adult Lymph Node	Lymph Node			Uni-ZAP XR
H0109	Human Macrophage, subtracted	Macrophage	Blood	Cell Line		pBluescript
H0110	Human Old Ovary, subtracted	Human Old Ovary	Ovary			pBluescript
H0111	Human Placenta, subtracted	Human Placenta	Placenta			pBluescript
H0116	Human Thymus Tumor, subtracted	Human Thymus Tumor	Thymus			pBluescript
H0118	Human Adult Kidney	Human Adult Kidney	Kidney			Uni-ZAP XR
H0120	Human Adult Spleen, subtracted	Human Adult Spleen	Spleen			Uni-ZAP XR
H0121	Human Cornea, subtracted	Human Cornea	eye			Uni-ZAP XR
H0122	Human Adult Skeletal Muscle	Human Skeletal Muscle	Sk Muscle			Uni-ZAP XR
H0123	Human Fetal Dura Mater	Human Fetal Dura Mater	Brain			Uni-ZAP XR
H0124	Human Rhabdomyosarcoma	Human Rhabdomyosarcoma	Sk Muscle	disease		Uni-ZAP XR
H0125	Cem cells cyclohexamide	Cyclohexamide Treated	Blood	Cell Line		Uni-ZAP XR

	treated	Cem, Jurkat, Raji, and Supt				
H0128	Jurkat cells, thiouridine activated	Jurkat Cells				Uni-ZAP XR
H0130	LNCAP untreated	LNCAP Cell Line	Prostate	Cell Line		Uni-ZAP XR
H0131	LNCAP + 0.3nM R1881	LNCAP Cell Line	Prostate	Cell Line		Uni-ZAP XR
H0132	LNCAP + 30nM R1881	LNCAP Cell Line	Prostate	Cell Line		Uni-ZAP XR
H0134	Raji Cells, cyclohexamide treated	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		Uni-ZAP XR
H0135	Human Synovial Sarcoma	Human Synovial Sarcoma	Synovium			Uni-ZAP XR
H0136	Supt Cells, cyclohexamide treated	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		Uni-ZAP XR
H0139	Activated T-Cells, 4 hrs.	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0140	Activated T-Cells, 8 hrs.	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0141	Activated T-Cells, 12 hrs.	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0144	Nine Week Old Early Stage Human	9 Wk Old Early Stage Human	Embryo			Uni-ZAP XR
H0147	Human Adult Liver	Human Adult Liver	Liver			Uni-ZAP XR
H0149	7 Week Old Early Stage Human, subtraced	Human Whole 7 Week Old Embryo	Embryo			Uni-ZAP XR
H0150	Human Epididymus	Epididymis	Testis			Uni-ZAP XR
H0151	Early Stage Human Liver	Human Fetal Liver	Liver			Uni-ZAP XR
H0154	Human Fibrosarcoma	Human Skin Fibrosarcoma	Skin		disease	Uni-ZAP XR
H0156	Human Adrenal Gland Tumor	Human Adrenal Gland Tumor	Adrenal Gland		disease	Uni-ZAP XR
H0158	Activated T-Cells, 4 hrs., ligation 2	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0159	Activated T-Cells, 8 hrs., ligation 2	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR

H0161	Activated T-Cells, 24 hrs., ligation 2	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0163	Human Synovium	Human Synovium	Synovium			Uni-ZAP XR
H0165	Human Prostate Cancer, Stage B2	Human Prostate Cancer, stage B2	Prostate		disease	Uni-ZAP XR
H0166	Human Prostate Cancer, Stage B2 fraction	Human Prostate Cancer, stage B2	Prostate		disease	Uni-ZAP XR
H0167	Activated T-Cells, 24 hrs.	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0169	Human Prostate Cancer, Stage C fraction	Human Prostate Cancer, stage C	Prostate		disease	Uni-ZAP XR
H0170	12 Week Old Early Stage Human	Twelve Week Old Early Stage Human	Embryo			Uni-ZAP XR
H0171	12 Week Old Early Stage Human, II	Twelve Week Old Early Stage Human	Embryo			Uni-ZAP XR
H0172	Human Fetal Brain, random primed	Human Fetal Brain	Brain			Lambda ZAP II
H0176	CAMAI Ee Cell Line	CAMAI Ee Cell Line	Breast	Cell Line		Uni-ZAP XR
H0177	CAMAI Ee Cell Line	CAMAI Ee Cell Line	Breast	Cell Line		Uni-ZAP XR
H0178	Human Fetal Brain	Human Fetal Brain	Brain			Uni-ZAP XR
H0179	Human Neutrophil	Human Neutrophil	Blood	Cell Line		Uni-ZAP XR
H0180	Human Primary Breast Cancer	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0181	Human Primary Breast Cancer	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0182	Human Primary Breast Cancer	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0183	Human Colon Cancer	Human Colon Cancer	Colon		disease	Uni-ZAP XR
H0184	Human Colon Cancer, metastaticized to live	Human Colon Cancer, metastaticized to liver	Liver		disease	Lambda ZAP II
H0187	Resting T-Cell	T-Cells	Blood	Cell Line		Lambda ZAP II
H0188	Human Normal Breast	Human Normal Breast	Breast			Uni-ZAP XR
H0189	Human Resting	Human	Blood	Cell Line		Uni-ZAP XR

	Macrophage	Macrophage/Monocytes			Cell Line		
H0190	Human Activated Macrophage (LPS)	Human Macrophage/Monocytes	Blood		Cell Line		Uni-ZAP XR
H0192	Cem Cells, cyclohexamide treated, subtra	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood		Cell Line		Uni-ZAP XR
H0194	Human Cerebellum, subtra	Human Cerebellum	Brain				pBluescript
H0196	Human Cardiomyopathy, subtra	Human Cardiomyopathy	Heart				Uni-ZAP XR
H0197	Human Fetal Liver, subtra	Human Fetal Liver	Liver				Uni-ZAP XR
H0199	Human Fetal Liver, subtra, neg clone	Human Fetal Liver	Liver				Uni-ZAP XR
H0200	Human Greater Omentum, fract II remake,	Human Greater Omentum	peritoneum				Uni-ZAP XR
H0201	Human Hippocampus, subtra	Human Hippocampus	Brain				pBluescript
H0202	Jurkat Cells, cyclohexamide treated, subtraction	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood		Cell Line		Uni-ZAP XR
H0204	Human Colon Cancer, subtra	Human Colon Cancer	Colon				pBluescript
H0205	Human Colon Cancer, differential	Human Colon Cancer	Colon				pBluescript
H0207	LNCAP, differential expression	LNCAP Cell Line	Prostate		Cell Line		pBluescript
H0208	Early Stage Human Lung, subtra	Human Fetal Lung	Lung				pBluescript
H0209	Human Cerebellum, differentially expressed	Human Cerebellum	Brain				Uni-ZAP XR
H0211	Human	Human Prostate	Prostate				pBluescript

	Prostate, differential expression						
H0212	Human Prostate, subtracted	Human Prostate	Prostate				pBluescript
H0213	Human Pituitary, subtracted	Human Pituitary					Uni-ZAP XR
H0214	Raji cells, cyclohexamide treated, subtracted	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line			pBluescript
H0215	Raji cells, cyclohexamide treated, differentially expressed	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line			pBluescript
H0216	Supt cells, cyclohexamide treated, subtracted	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line			pBluescript
H0217	Supt cells, cyclohexamide treated, differentially expressed	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line			pBluescript
H0218	Activated T-Cells, 0hrs, subtracted	Activated T-Cells	Blood	Cell Line			Uni-ZAP XR
H0219	Activated T-Cells, 0hrs, differentially expressed	Activated T-Cells	Blood	Cell Line			Uni-ZAP XR
H0220	Activated T-Cells, 4 hrs, subtracted	Activated T-Cells	Blood	Cell Line			Uni-ZAP XR
H0222	Activated T-Cells, 8 hrs, subtracted	Activated T-Cells	Blood	Cell Line			Uni-ZAP XR
H0223	Activated T-Cells, 8 hrs, differentially expressed	Activated T-Cells	Blood	Cell Line			Uni-ZAP XR
H0224	Activated T-Cells, 12 hrs, subtracted	Activated T-Cells	Blood	Cell Line			Uni-ZAP XR
H0225	Activated T-Cells, 12hrs, differentially expressed	Activated T-Cells	Blood	Cell Line			Uni-ZAP XR
H0229	Early Stage Human	Early Stage Human Brain	Brain				Lambda ZAP II

	Brain, random primed	Human Cardiomyopathy	Heart		disease	Uni-ZAP XR
H0230	Human Cardiomyopathy, diff exp	Human Colon				pBluescript
H0231	Human Colon, subtraction	Human Colon				pBluescript
H0232	Human Colon, differential expression	Human Colon				pBluescript
H0234	human colon cancer, metastatic to liver, differentially expressed	Human Colon Cancer, metastaticized to liver	Liver			pBluescript
H0235	Human colon cancer, metastaticized to liver, subtraction	Human Colon Cancer, metastaticized to liver	Liver			pBluescript
H0239	Human Kidney Tumor	Human Kidney Tumor	Kidney		disease	Uni-ZAP XR
H0240	C7MCF7 cell line, estrogen treated, Differential	C7MCF7 Cell Line, estrogen treated	Breast	Cell Line		Uni-ZAP XR
H0241	C7MCF7 cell line, estrogen treated, subtraction	C7MCF7 Cell Line, estrogen treated	Breast	Cell Line		Uni-ZAP XR
H0242	Human Fetal Heart, Differential (Fetal-Specific)	Human Fetal Heart	Heart			pBluescript
H0244	Human 8 Week Whole Embryo, subtracted	Human 8 Week Old Embryo	Embryo			Uni-ZAP XR
H0246	Human Fetal Liver-Enzyme subtraction	Human Fetal Liver	Liver			Uni-ZAP XR
H0247	Human Membrane Bound Polysomes-Enzyme Subtraction	Human Membrane Bound Polysomes	Blood	Cell Line		Uni-ZAP XR
H0249	HE7, subtracted by hybridization with E7 cDNA	Human Whole 7 Week Old Embryo	Embryo			Uni-ZAP XR

H0250	Human Activated Monocytes	Human Monocytes					Uni-ZAP XR
H0251	Human Chondrosarcoma	Human Chondrosarcoma	Cartilage		disease		Uni-ZAP XR
H0252	Human Osteosarcoma	Human Osteosarcoma	Bone		disease		Uni-ZAP XR
H0253	Human adult testis, large inserts	Human Adult Testis	Testis				Uni-ZAP XR
H0254	Breast Lymph node cDNA library	Breast Lymph Node	Lymph Node				Uni-ZAP XR
H0255	breast lymph node CDNA library	Breast Lymph Node	Lymph Node				Lambda ZAP II
H0256	HL-60, unstimulated	Human HL-60 Cells, unstimulated	Blood	Cell Line			Uni-ZAP XR
H0257	HL-60, PMA 4H	HL-60 Cells, PMA stimulated 4H	Blood	Cell Line			Uni-ZAP XR
H0261	H. cerebellum, Enzyme subtracted	Human Cerebellum	Brain				Uni-ZAP XR
H0263	human colon cancer	Human Colon Cancer	Colon		disease		Lambda ZAP II
H0264	human tonsils	Human Tonsil	Tonsil				Uni-ZAP XR
H0265	Activated T-Cell (12hs)/Thiouridine labelledEco	T-Cells	Blood	Cell Line			Uni-ZAP XR
H0266	Human Microvascular Endothelial Cells, fract. A	HMEC	Vein	Cell Line			Lambda ZAP II
H0267	Human Microvascular Endothelial Cells, fract. B	HMEC	Vein	Cell Line			Lambda ZAP II
H0268	Human Umbilical Vein Endothelial Cells, fract. A	HUVE Cells	Umbilical vein	Cell Line			Lambda ZAP II
H0269	Human Umbilical Vein Endothelial Cells, fract. B	HUVE Cells	Umbilical vein	Cell Line			Lambda ZAP II

H0270	HPAS (human pancreas, subtracted)	Human Pancreas	Pancreas			Uni-ZAP XR
H0271	Human Neutrophil, Activated	Human Neutrophil - Activated	Blood	Cell Line		Uni-ZAP XR
H0272	HUMAN TONSILS, FRACTION 2	Human Tonsil	Tonsil			Uni-ZAP XR
H0274	Human Adult Spleen, fraction II	Human Adult Spleen	Spleen			Uni-ZAP XR
H0275	Human Infant Adrenal Gland, Subtracted	Human Infant Adrenal Gland	Adrenal gland			pBluescript
H0280	K562 + PMA (36 hrs)	K562 Cell line	cell line	Cell Line		ZAP Express
H0281	Lymph node, abnorm. cell line (ATCC #7225)	Lymph Node, abnormal cell line	Lymph Node	Cell Line		ZAP Express
H0282	HBGB's differential consolidation	Human Primary Breast Cancer	Breast			Uni-ZAP XR
H0284	Human OB MG63 control fraction I	Human Osteoblastoma MG63 cell line	Bone	Cell Line		Uni-ZAP XR
H0286	Human OB MG63 treated (10 nM E2) fraction I	Human Osteoblastoma MG63 cell line	Bone	Cell Line		Uni-ZAP XR
H0288	Human OB HOS control fraction I	Human Osteoblastoma HOS cell line	Bone	Cell Line		Uni-ZAP XR
H0290	Human OB HOS treated (1 nM E2) fraction I	Human Osteoblastoma HOS cell line	Bone	Cell Line		Uni-ZAP XR
H0292	Human OB HOS treated (10 nM E2) fraction I	Human Osteoblastoma HOS cell line	Bone	Cell Line		Uni-ZAP XR
H0293	WT 38 cells					Uni-ZAP XR
H0294	Amniotic Cells - TNF induced	Amniotic Cells - TNF induced	Placenta	Cell Line		Uni-ZAP XR
H0295	Amniotic Cells - Primary Culture	Amniotic Cells - Primary Culture	Placenta	Cell Line		Uni-ZAP XR
H0300	CD34 positive cells (Cord Blood)	CD34 Positive Cells	Cord Blood			ZAP Express

H0305	CD34 positive cells (Cord Blood)	CD34 Positive Cells	Cord Blood			ZAP Express
H0306	CD34 depleted Buffy Coat (Cord Blood)	CD34 Depleted Buffy Coat (Cord Blood)	Cord Blood			ZAP Express
H0309	Human Chronic Synovitis	Synovium, Chronic Synovitis/ Osteoarthritis	Synovium		disease	Uni-ZAP XR
H0310	human caudate nucleus	Brain	Brain			Uni-ZAP XR
H0316	HUMAN STOMACH	Human Stomach	Stomach			Uni-ZAP XR
H0318	HUMAN B CELL LYMPHOMA	Human B Cell Lymphoma	Lymph Node		disease	Uni-ZAP XR
H0320	Human frontal cortex	Human Frontal Cortex	Brain			Uni-ZAP XR
H0321	HUMAN SCHWANOMA	Schwannoma	Nerve		disease	Uni-ZAP XR
H0327	human corpus colosum	Human Corpus Callosum	Brain			Uni-ZAP XR
H0328	human ovarian cancer	Ovarian Cancer	Ovary		disease	Uni-ZAP XR
H0329	Dermatofibrosarcoma Protuberance	Dermatofibrosarcoma Protuberans	Skin		disease	Uni-ZAP XR
H0331	Hepatocellular Tumor	Hepatocellular Tumor	Liver		disease	Lambda ZAP II
H0333	Hemangiopericytoma	Hemangiopericytoma	Blood vessel		disease	Lambda ZAP II
H0334	Kidney cancer	Kidney Cancer	Kidney		disease	Uni-ZAP XR
H0339	Duodenum	Duodenum				Uni-ZAP XR
H0341	Bone Marrow Cell Line (RS4;11)	Bone Marrow Cell Line RS4;11	Bone Marrow	Cell Line		Uni-ZAP XR
H0342	Lingual Gyrus	Lingual Gyrus	Brain			Uni-Zap XR
H0343	stomach cancer (human)	Stomach Cancer - 5383A (human)			disease	Uni-ZAP XR
H0344	Adipose tissue (human)	Adipose - 6825A (human)				Uni-ZAP XR
H0345	SKIN	Skin - 4000868H	Skin			Uni-ZAP XR
H0346	Brain-medulloblastoma	Brain (Medulloblastoma)- 9405C006R	Brain		disease	Uni-ZAP XR
H0349	human adult liver cDNA library	Human Adult Liver	Liver			pCMVSPORT 1
H0350	Human Fetal Liver,	Human Fetal Liver, mixed	Liver			Uni-ZAP XR

	mixed 10 & 14 week	10&14 Week					
H0351	Glioblastoma	Glioblastoma	Brain		disease	Uni-ZAP XR	
H0352	wilm's tumor	Wilm's Tumor			disease	Uni-ZAP XR	
H0354	Human Leukocytes	Human Leukocytes	Blood	Cell Line		pCMVSPORT 1	
H0355	Human Liver	Human Liver, normal Adult				pCMVSPORT 1	
H0356	Human Kidney	Human Kidney	Kidney			pCMVSPORT 1	
H0357	H. Normalized Fetal Liver, II	Human Fetal Liver	Liver			Uni-ZAP XR	
H0359	KMH2 cell line	KMH2				ZAP Express	
H0360	Hemangiopericytoma	Hemangiopericytoma			disease		
H0361	Human rejected kidney	Human Rejected Kidney			disease	pBluescript	
H0362	HeLa cell line	HELA CELL LINE				pSport1	
H0366	L428 cell line	L428				ZAP Express	
H0369	H. Atrophic Endometrium	Atrophic Endometrium and myometrium				Uni-ZAP XR	
H0370	H. Lymph node breast Cancer	Lymph node with Met. Breast Cancer			disease	Uni-ZAP XR	
H0372	Human Testes	Human Testes	Testis			pCMVSPORT 1	
H0373	Human Heart	Human Adult Heart	Heart			pCMVSPORT 1	
H0374	Human Brain	Human Brain				pCMVSPORT 1	
H0375	Human Lung	Human Lung				pCMVSPORT 1	
H0376	Human Spleen	Human Adult Spleen	Spleen			pCMVSPORT 1	
H0379	Human Tongue, frac 1	Human Tongue				pSport1	
H0380	Human Tongue, frac 2	Human Tongue				pSport1	
H0381	Bone Cancer	Bone Cancer			disease	Uni-ZAP XR	
H0383	Human Prostate BPH, re-excision	Human Prostate BPH				Uni-ZAP XR	
H0384	Brain, Kozak	Human Brain				pCMVSPORT 1	
H0386	Leukocyte and Lung; 4 screens	Human Leukocytes	Blood	Cell Line		pCMVSPORT 1	
H0388	Human Rejected Kidney,	Human Rejected Kidney			disease	pBluescript	

	704 re-excision					disease	pBluescript
H0390	Human Amygdala Depression, re-excision	Human Amygdala Depression					pBluescript
H0391	H. Meningima, M6	Human Meningima	brain				pSport1
H0392	H. Meningima, M1	Human Meningima	brain				pSport1
H0393	Fetal Liver, subtraction II	Human Fetal Liver	Liver				pBluescript
H0394	A-14 cell line	Redd-Sternberg cell					ZAP Express
H0395	A1-CELL LINE	Redd-Sternberg cell					ZAP Express
H0396	L1 Cell line	Redd-Sternberg cell					ZAP Express
H0399	Human Kidney Cortex, re-rescue	Human Kidney Cortex					Lambda ZAP II
H0400	Human Striatum Depression, re-rescue	Human Brain, Striatum Depression	Brain				Lambda ZAP II
H0402	CD34 depleted Buffy Coat (Cord Blood), re-excision	CD34 Depleted Buffy Coat (Cord Blood)	Cord Blood				ZAP Express
H0403	H. Umbilical Vein Endothelial Cells, IL4 induced	HUVE Cells	Umbilical vein		Cell Line		Uni-ZAP XR
H0404	H. Umbilical Vein endothelial cells, uninduced	HUVE Cells	Umbilical vein		Cell Line		Uni-ZAP XR
H0405	Human Pituitary, subtracted VI	Human Pituitary					pBluescript
H0406	H Amygdala Depression, subtracted	Human Amygdala Depression					Uni-ZAP XR
H0408	Human kidney Cortex, subtracted	Human Kidney Cortex					pBluescript
H0409	H. Striatum Depression, subtracted	Human Brain, Striatum Depression	Brain				pBluescript
H0410	H. Male bladder, adult	H Male Bladder, Adult	Bladder				pSport1
H0411	H Female Bladder, Adult	Human Female Adult Bladder	Bladder				pSport1

H0412	Human umbilical vein endothelial cells, IL-4 induced	HUVE Cells	Umbilical vein	Cell Line		pSport1
H0413	Human Umbilical Vein Endothelial Cells, uninduced	HUVE Cells	Umbilical vein	Cell Line		pSport1
H0414	Ovarian Tumor I, OV5232	Ovarian Tumor, OV5232	Ovary		disease	pSport1
H0415	H. Ovarian Tumor, II, OV5232	Ovarian Tumor, OV5232	Ovary		disease	pCMVSPORT 2.0
H0416	Human Neutrophils, Activated, re-excision	Human Neutrophil - Activated	Blood	Cell Line		pBluescript
H0417	Human Pituitary, subtracted VIII	Human Pituitary				pBluescript
H0418	Human Pituitary, subtracted VII	Human Pituitary				pBluescript
H0419	Bone Cancer, re-excision	Bone Cancer				Uni-ZAP XR
H0421	Human Bone Marrow, re-excision	Bone Marrow				pBluescript
H0422	T-Cell PHA 16 hrs	T-Cells	Blood	Cell Line		pSport1
H0423	T-Cell PHA 24 hrs	T-Cells	Blood	Cell Line		pSport1
H0424	Human Pituitary, subt IX	Human Pituitary				pBluescript
H0427	Human Adipose	Human Adipose, left hipipoma				pSport1
H0428	Human Ovary	Human Ovary Tumor	Ovary			pSport1
H0429	K562 + PMA (36 hrs), re-excision	K562 Cell line	cell line	Cell Line		ZAP Express
H0431	H. Kidney Medulla, re-excision	Kidney medulla	Kidney			pBluescript
H0433	Human Umbilical Vein Endothelial cells, frac B, re-excision	HUVE Cells	Umbilical vein	Cell Line		pBluescript
H0434	Human Brain, striatum,	Human Brain, Striatum				pBluescript

	re-excision	Ovarian Tumor, OV350721	Ovary				
H0435	Ovarian Tumor 10-3-95	Ovarian Tumor, OV350721	Ovary				pCMVSPORT 2.0
H0436	Resting T-Cell Library, II	T-Cells	Blood		Cell Line		pSport1
H0437	H Umbilical Vein Endothelial Cells, frac A, re-excision	HUVE Cells	Umbilical vein		Cell Line		Lambda ZAP II
H0438	H. Whole Brain #2, re-excision	Human Whole Brain #2					ZAP Express
H0439	Human Eosinophils	Eosinophils					pBluescript
H0441	H. Kidney Cortex, subtracted	Kidney cortex	Kidney				pBluescript
H0443	H. Adipose, subtracted	Human Adipose, left hiplipoma					pSport1
H0444	Spleen metastatic melanoma	Spleen, Metastatic malignant melanoma	Spleen			disease	pSport1
H0445	Spleen, Chronic lymphocytic leukemia	Human Spleen, CLL	Spleen			disease	pSport1
H0449	CD34+ cell, I	CD34 positive cells					pSport1
H0455	H. Striatum Depression, subt	Human Brain, Striatum Depression	Brain				pBluescript
H0457	Human Eosinophils	Human Eosinophils					pSport1
H0458	CD34+ cell, I, frac II	CD34 positive cells					pSport1
H0459	CD34+cells, II, FRACTION 2	CD34 positive cells					pCMVSPORT 2.0
H0461	H. Kidney Medulla, subtracted	Kidney medulla	Kidney				pBluescript
H0462	H. Amygdala Depression, subtracted		Brain				pBluescript
H0477	Human Tonsil, Lib 3	Human Tonsil	Tonsil				pSport1
H0478	Salivary Gland, Lib 2	Human Salivary Gland	Salivary gland				pSport1
H0479	Salivary Gland, Lib 3	Human Salivary Gland	Salivary gland				pSport1
H0483	Breast Cancer cell line,	Breast Cancer Cell line,					pSport1

	MDA 36	MDA 36					
H0484	Breast Cancer Cell line, angiogenic	Breast Cancer Cell line, Angiogenic, 36T3					pSport1
H0485	Hodgkin's Lymphoma I	Hodgkin's Lymphoma I				disease	pCMVSPORT 2.0
H0486	Hodgkin's Lymphoma II	Hodgkin's Lymphoma II				disease	pCMVSPORT 2.0
H0487	Human Tonsils, lib 1	Human Tonsils					pCMVSPORT 2.0
H0488	Human Tonsils, Lib 2	Human Tonsils					pCMVSPORT 2.0
H0489	Crohn's Disease	Ileum	Intestine			disease	pSport1
H0490	HL-60, untreated, subtracted	Human HL-60 Cells, unstimulated	Blood		Cell Line		Uni-ZAP XR
H0491	HL-60, PMA 4H, subtracted	HL-60 Cells, PMA stimulated 4H	Blood		Cell Line		Uni-ZAP XR
H0492	HL-60, RA 4h, Subtracted	HL-60 Cells, RA stimulated for 4H	Blood		Cell Line		Uni-ZAP XR
H0494	Keratinocyte	Keratinocyte					pCMVSPORT 2.0
H0497	HEL cell line	HEL cell line			HEL 92.1.7		pSport1
H0505	Human Astrocyte	Human Astrocyte					pSport1
H0506	Ulcerative Colitis	Colon	Colon				pSport1
H0509	Liver, Hepatoma	Human Liver, Hepatoma, patient 8	Liver			disease	pCMVSPORT 3.0
H0510	Human Liver, normal	Human Liver, normal, Patient # 8	Liver				pCMVSPORT 3.0
H0512	Keratinocyte, lib 3	Keratinocyte					pCMVSPORT 2.0
H0518	pBMC stimulated w/ poly I/C	pBMC stimulated with poly I/C					pCMVSPORT 3.0
H0519	NTERA2, control	NTERA2, Teratocarcinoma cell line					pCMVSPORT 3.0
H0520	NTERA2 + retinoic acid, 14 days	NTERA2, Teratocarcinoma cell line					pSport1
H0521	Primary Dendritic Cells, lib 1	Primary Dendritic cells					pCMVSPORT 3.0
H0522	Primary Dendritic cells, frac 2	Primary Dendritic cells					pCMVSPORT 3.0

H0525	PCR, pBMC I/C treated	pBMC stimulated with poly I/C					PCRII
H0528	Poly[I]/Poly[C] Normal Lung Fibroblasts	Poly[I]/Poly[C] Normal Lung Fibroblasts					pCMVSPORT 3.0
H0529	Myeloid Progenitor Cell Line	TF-1 Cell Line; Myeloid progenitor cell line					pCMVSPORT 3.0
H0530	Human Dermal Endothelial Cells, untreated	Human Dermal Endothelial Cells; untreated					pSPORT1
H0538	Merkel Cells	Merkel cells	Lymph node				pSPORT1
H0539	Pancreas Islet Cell Tumor	Pancreas Islet Cell Tumor	Pancreas			disease	pSPORT1
H0540	Skin, burned	Skin, leg burned	Skin				pSPORT1
H0542	T Cell helper I	Helper T cell					pCMVSPORT 3.0
H0543	T cell helper II	Helper T cell					pCMVSPORT 3.0
H0544	Human endometrial stromal cells	Human endometrial stromal cells					pCMVSPORT 3.0
H0545	Human endometrial stromal cells-treated with progesterone	Human endometrial stromal cells-treated with proge					pCMVSPORT 3.0
H0546	Human endometrial stromal cells-treated with estradiol	Human endometrial stromal cells-treated with estro					pCMVSPORT 3.0
H0547	NTERA2 teratocarcinoma cell line+retinoic acid (14 days)	NTERA2, Teratocarcinoma cell line					pSPORT1
H0549	H. Epididymus, caput & corpus	Human Epididymus, caput and corpus					Uni-ZAP XR
H0550	H. Epididymus, cauda	Human Epididymus, cauda					Uni-ZAP XR
H0551	Human Thymus Stromal Cells	Human Thymus Stromal Cells					pCMVSPORT 3.0

H0553	Human Placenta	Human Placenta	Kidney	Cell Line	disease	pCMV Sport 3.0
H0555	Rejected Kidney, lib 4	Human Rejected Kidney	Kidney			pCMV Sport 3.0
H0556	Activated T-cell (12h)/Thiouridine-re-excision	T-Cells	Blood			Uni-ZAP XR
H0559	HL-60, PMA 4H, re-excision	HL-60 Cells, PMA stimulated 4H	Blood	Cell Line		Uni-ZAP XR
H0560	KMH2	KMH2				
H0561	L428	L428				
H0562	Human Fetal Brain, normalized c5-11-26	Human Fetal Brain				pCMV Sport 3.0
H0563	Human Fetal Brain, normalized 50021F	Human Fetal Brain				pCMV Sport 3.0
H0564	Human Fetal Brain, normalized C5001F	Human Fetal Brain				pCMV Sport 2.0
H0566	Human Fetal Brain, normalized c50F	Human Fetal Brain				pCMV Sport 2.0
H0567	Human Fetal Brain, normalized A5002F	Human Fetal Brain				pCMV Sport 2.0
H0569	Human Fetal Brain, normalized CO	Human Fetal Brain				pCMV Sport 2.0
H0570	Human Fetal Brain, normalized C500H	Human Fetal Brain				pCMV Sport 2.0
H0571	Human Fetal Brain, normalized C500HE	Human Fetal Brain				pCMV Sport 2.0
H0572	Human Fetal Brain, normalized AC5002	Human Fetal Brain				pCMV Sport 2.0
H0574	Hepatocellular Tumor; re-excision	Hepatocellular Tumor	Liver			pCMV Sport 2.0
H0575	Human Adult Pulmonary; re-excision	Human Adult Pulmonary	Lung		disease	Lambda ZAP II
H0576	Resting T-Cell; re-excision	T-Cells	Blood	Cell Line		Uni-ZAP XR
						Lambda ZAP II

H0580	Dendritic cells, pooled	Pooled dendritic cells				pCMVSPORT 3.0
H0581	Human Bone Marrow, treated	Human Bone Marrow	Bone Marrow			pCMVSPORT 3.0
H0583	B Cell lymphoma	B Cell Lymphoma	B Cell		disease	pCMVSPORT 3.0
H0584	Activated T-cells, 24 hrs, re-excision	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0585	Activated T-Cells, 12 hrs, re-excision	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0586	Healing groin wound, 6.5 hours post incision	healing groin wound, 6.5 hours post incision - 2/	groin		disease	pCMVSPORT 3.0
H0587	Healing groin wound; 7.5 hours post incision	Groin-2/19/97	groin		disease	pCMVSPORT 3.0
H0589	CD34 positive cells (cord blood), re-ex	CD34 Positive Cells	Cord Blood			ZAP Express
H0590	Human adult small intestine, re-excision	Human Adult Small Intestine	Small Int.			Uni-ZAP XR
H0591	Human T-cell lymphoma; re-excision	T-Cell Lymphoma	T-Cell		disease	Uni-ZAP XR
H0592	Healing groin wound - zero hr post-incision (control)	HGS wound healing project; abdomen			disease	pCMVSPORT 3.0
H0593	Olfactory epithelium; nasal cavity	Olfactory epithelium from roof of left nasal cavity				pCMVSPORT 3.0
H0594	Human Lung Cancer; re-excision	Human Lung Cancer	Lung		disease	Lambda ZAP II
H0595	Stomach cancer (human); re-excision	Stomach Cancer - 5383A (human)			disease	Uni-ZAP XR
H0596	Human Colon Cancer; re-excision	Human Colon Cancer	Colon			Lambda ZAP II
H0597	Human Colon; re-excision	Human Colon				Lambda ZAP II
H0598	Human Stomach; re-excision	Human Stomach	Stomach			Uni-ZAP XR

H0599	Human Adult Heart; re-excision	Human Adult Heart	Heart			Uni-ZAP XR
H0600	Healing Abdomen wound; 70&90 min post incision	Abdomen			disease	pCMV Sport 3.0
H0601	Healing Abdomen Wound; 15 days post incision	Abdomen			disease	pCMV Sport 3.0
H0602	Healing Abdomen Wound; 21&29 days post incision	Abdomen			disease	pCMV Sport 3.0
H0604	Human Pituitary, re-excision	Human Pituitary				pBluescript
H0606	Human Primary Breast Cancer; re-excision	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0607	H. Leukocytes, normalized cot 50A3	H. Leukocytes				pCMV Sport 1
H0609	H. Leukocytes, normalized cot > 500A	H. Leukocytes				pCMV Sport 1
H0611	H. Leukocytes, normalized cot 500 B	H. Leukocytes				pCMV Sport 1
H0613	H. Leukocytes, normalized cot 5B	H. Leukocytes				pCMV Sport 1
H0614	H. Leukocytes, normalized cot 500 A	H. Leukocytes				pCMV Sport 1
H0615	Human Ovarian Cancer Reexcision	Ovarian Cancer	Ovary		disease	Uni-ZAP XR
H0616	Human Testes, Reexcision	Human Testes	Testis			Uni-ZAP XR
H0617	Human Primary Breast Cancer Reexcision	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0618	Human Adult Testes, Large Inserts, Reexcision	Human Adult Testis	Testis			Uni-ZAP XR

H0619	Fetal Heart	Human Fetal Heart	Heart			Uni-ZAP XR
H0620	Human Fetal Kidney; Reexcision	Human Fetal Kidney	Kidney			Uni-ZAP XR
H0622	Human Pancreas Tumor; Reexcision	Human Pancreas Tumor	Pancreas		disease	Uni-ZAP XR
H0623	Human Umbilical Vein; Reexcision	Human Umbilical Vein Endothelial Cells	Umbilical vein			Uni-ZAP XR
H0624	12 Week Early Stage Human II; Reexcision	Twelve Week Old Early Stage Human	Embryo			Uni-ZAP XR
H0625	Ku 812F Basophils Line	Ku 812F Basophils				pSport1
H0626	Saos2 Cells; Untreated	Saos2 Cell Line; Untreated				pSport1
H0627	Saos2 Cells; Vitamin D3 Treated	Saos2 Cell Line; Vitamin D3 Treated				pSport1
H0628	Human Pre-Differentiated Adipocytes	Human Pre-Differentiated Adipocytes				Uni-ZAP XR
H0629	Human Leukocyte, control #2	Human Normalized leukocyte				pCMVSPORT 1
H0631	Saos2, Dexamethosone Treated	Saos2 Cell Line; Dexamethosone Treated				pSport1
H0632	Hepatocellular Tumor; re-excision	Hepatocellular Tumor	Liver			Lambda ZAP II
H0633	Lung Carcinoma A549 TNFalpha activated	TNFalpha activated A549-Lung Carcinoma			disease	pSport1
H0634	Human Testes Tumor, re-excision	Human Testes Tumor	Testis		disease	Uni-ZAP XR
H0635	Human Activated T-Cells, re-excision	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0637	Dendritic Cells From CD34 Cells	Dendritic cells from CD34 cells				pSport1
H0638	CD40 activated monocyte dendritic cells	CD40 activated monocyte dendritic cells				pSport1
H0640	Ficoll Human Stromal	Ficoll Human Stromal				Other

	Cells, Untreated	Cells, Untreated					
H0641	LPS activated derived dendritic cells	LPS activated monocyte derived dendritic cells					pSport1
H0642	Hep G2 Cells, lambda library	Hep G2 Cells					Other
H0643	Hep G2 Cells, PCR library	Hep G2 Cells					Other
H0644	Human Placenta (re-excision)	Human Placenta	Placenta				Uni-ZAP XR
H0645	Fetal Heart, re-excision	Human Fetal Heart	Heart				Uni-ZAP XR
H0646	Lung, Cancer (4005313 A3): Invasive Poorly Differentiated Lung Adenocarcinoma,	Metastatic squamous cell lung carcinoma, poorly di					pSport1
H0647	Lung, Cancer (4005163 B7): Invasive, Poorly Diff. Adenocarcinoma, Metastatic	Invasive poorly differentiated lung adenocarcinoma			disease		pSport1
H0648	Ovary, Cancer: (4004562 B6) Papillary Serous Cystic Neoplasm, Low Malignant Pot	Papillary Cstic neoplasm of low malignant potentia			disease		pSport1
H0649	Lung, Normal: (4005313 B1)	Normal Lung					pSport1
H0650	B-Cells	B-Cells					pCMVSPORT 3.0
H0651	Ovary, Normal: (9805C040R)	Normal Ovary					pSport1
H0652	Lung, Normal: (4005313 B1)	Normal Lung					pSport1
H0653	Stromal Cells	Stromal Cells					pSport1
H0654	Lung, Cancer: (4005313 A3) Invasive Poorly-differentiated Metastatic	Metastatic Squamous cell lung Carcinoma poorly dif					pSport1
							Other

	lung adenoc							
H0656	B-cells (unstimulated)	B-cells (unstimulated)						pSport1
H0657	B-cells (stimulated)	B-cells (stimulated)						pSport1
H0658	Ovary, Cancer (9809C332): Poorly differentiated adenocarcinoma	9809C332- Poorly differentiate	Ovary & Fallopian Tubes			disease		pSport1
H0659	Ovary, Cancer (15395A1F): Grade II Papillary Carcinoma	Grade II Papillary Carcinoma, Ovary	Ovary			disease		pSport1
H0660	Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma	Poorly differentiated carcinoma, ovary				disease		pSport1
H0661	Breast, Cancer: (4004943 A5)	Breast cancer				disease		pSport1
H0662	Breast, Normal: (4005522B2)	Normal Breast - #4005522(B2)	Breast					pSport1
H0663	Breast, Cancer: (4005522 A2)	Breast Cancer - #4005522(A2)	Breast			disease		pSport1
H0664	Breast, Cancer: (9806C012R)	Breast Cancer	Breast			disease		pSport1
H0665	Stromal cells 3.88	Stromal cells 3.88						pSport1
H0666	Ovary, Cancer: (4004332 A2)	Ovarian Cancer, Sample #4004332A2				disease		pSport1
H0667	Stromal cells(HBM3.18)	Stromal cell(HBM 3.18)						pSport1
H0668	stromal cell clone 2.5	stromal cell clone 2.5						pSport1
H0669	Breast, Cancer: (4005385 A2)	Breast Cancer (4005385A2)	Breast					pSport1
H0670	Ovary, Cancer(4004650 A3): Well-Differentiated Micropapillary Serous Carcinoma	Ovarian Cancer - 4004650A3						pSport1

H0671	Breast, Cancer: (9802C02OE)	Breast Cancer- Sample # 9802C02OE				pSportI
H0672	Ovary, Cancer: (4004576A8)	Ovarian Cancer(4004576A8)	Ovary			pSportI
H0673	Human Prostate Cancer, Stage B2; re-excision	Human Prostate Cancer, stage B2	Prostate			Uni-ZAP XR
H0674	Human Prostate Cancer, Stage C; re-excision	Human Prostate Cancer, stage C	Prostate			Uni-ZAP XR
H0675	Colon, Cancer: (9808C064R)	Colon Cancer 9808C064R				pCMVSPORT 3.0
H0676	Colon, Cancer: (9808C064R)-total RNA	Colon Cancer 9808C064R				pCMVSPORT 3.0
H0677	TNFR degenerate oligo	B-Cells				PCRII
H0678	screened clones from placental library	Placenta	Placenta			Other
H0682	Serous Papillary Adenocarcinoma	serous papillary adenocarcinoma (9606G304SPA3B)				pCMVSPORT 3.0
H0683	Ovarian Serous Papillary Adenocarcinoma	Serous papillary adenocarcinoma, stage 3C (9804G01)				pCMVSPORT 3.0
H0684	Serous Papillary Adenocarcinoma	Ovarian Cancer-9810G606	Ovaries			pCMVSPORT 3.0
H0685	Adenocarcinoma of Ovary, Human Cell Line, # OVCAR-3	Adenocarcinoma of Ovary, Human Cell Line, # OVCAR-				pCMVSPORT 3.0
H0686	Adenocarcinoma of Ovary, Human Cell Line	Adenocarcinoma of Ovary, Human Cell Line, # SW-626				pCMVSPORT 3.0
H0687	Human normal ovary(#9610G215)	Human normal ovary(#9610G215)	Ovary			pCMVSPORT 3.0
H0688	Human Ovarian Cancer(#9807G017)	Human Ovarian cancer(#9807G017),mRN				pCMVSPORT 3.0

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H0689	Ovarian Cancer		Ovarian Cancer, #9806G019					pCMV Sport 3.0
H0690	Ovarian Cancer, #9702G001		Ovarian Cancer, #9702G001					pCMV Sport 3.0
H0691	Normal Ovary, #9710G208		normal ovary, #9710G208					pCMV Sport 3.0
H0693	Normal Prostate #ODQ3958EN		Normal Prostate Tissue # ODQ3958EN					pCMV Sport 3.0
H0694	Prostate gland adenocarcinoma		Prostate gland, adenocarcinoma, mod/diff, gleason	prostate gland				pCMV Sport 3.0
H0695	mononucleocytes from patient		mononucleocytes from patient at Shady Grove Hospital					pCMV Sport 3.0
N0003	Human Fetal Brain		Human Fetal Brain					
N0006	Human Fetal Brain		Human Fetal Brain					
N0007	Human Hippocampus		Human Hippocampus					
N0009	Human Hippocampus, prescreened		Human Hippocampus					
S0001	Brain frontal cortex		Brain frontal cortex	Brain				Lambda ZAP II
S0002	Monocyte activated		Monocyte-activated	blood	Cell Line			Uni-ZAP XR
S0003	Human Osteoclastoma		Osteoclastoma	bone		disease		Uni-ZAP XR
S0004	Prostate		Prostate BPH	Prostate				Lambda ZAP II
S0005	Heart		Heart-left ventricle	Heart				pCDNA
S0006	Neuroblastoma		Human Neural Blastoma			disease		pCDNA
S0007	Early Stage Human Brain		Human Fetal Brain					Uni-ZAP XR
S0010	Human Amygdala		Amygdala					Uni-ZAP XR
S0011	STROMAL - OSTEOCLASTOMA		Osteoclastoma	bone		disease		Uni-ZAP XR
S0013	Prostate		Prostate	prostate				Uni-ZAP XR
S0014	Kidney Cortex		Kidney cortex	Kidney				Uni-ZAP XR
S0015	Kidney medulla		Kidney medulla	Kidney				Uni-ZAP XR

S0016	Kidney Pyramids	Kidney pyramids	Kidney			Uni-ZAP XR
S0021	Whole brain	Whole brain	Brain			ZAP Express
S0022	Human Osteoclastoma Stromal Cells - unamplified	Osteoclastoma Stromal Cells				Uni-ZAP XR
S0024	Human Kidney Medulla - unamplified	Human Kidney Medulla				
S0026	Stromal cell TF274	stromal cell	Bone marrow		Cell Line	Uni-ZAP XR
S0027	Smooth muscle, serum treated	Smooth muscle	Pulmonary artery		Cell Line	Uni-ZAP XR
S0028	Smooth muscle, control	Smooth muscle	Pulmonary artery		Cell Line	Uni-ZAP XR
S0029	Brain stem	Brain stem	brain			Uni-ZAP XR
S0030	Brain pons	Brain Pons	Brain			Uni-ZAP XR
S0031	Spinal cord	Spinal cord	spinal cord			Uni-ZAP XR
S0032	Smooth muscle-IL1b induced	Smooth muscle	Pulmonary artery		Cell Line	Uni-ZAP XR
S0035	Brain medulla oblongata	Brain medulla oblongata				Uni-ZAP XR
S0036	Human Substantia Nigra	Human Substantia Nigra	Brain			Uni-ZAP XR
S0037	Smooth muscle, IL1b induced	Smooth muscle	Pulmonary artery		Cell Line	Uni-ZAP XR
S0038	Human Whole Brain #2 - Oligo dT > 1.5Kb	Human Whole Brain #2				ZAP Express
S0039	Hypothalamus	Hypothalamus	Brain			Uni-ZAP XR
S0040	Adipocytes	Human Adipocytes from Osteoclastoma				Uni-ZAP XR
S0042	Testes	Human Testes				ZAP Express
S0044	Prostate BPH	prostate BPH	Prostate		disease	Uni-ZAP XR
S0045	Endothelial cells-control	Endothelial cell	endothelial cell-lung		Cell Line	Uni-ZAP XR
S0046	Endothelial-induced	Endothelial cell	endothelial cell-lung		Cell Line	Uni-ZAP XR
S0048	Human Hypothalamus, Alzheimer's	Human Hypothalamus, Alzheimer's			disease	Uni-ZAP XR

S0049	Human Brain, Striatum	Human Brain, Striatum					Uni-ZAP XR
S0050	Human Frontal Cortex, Schizophrenia	Human Frontal Cortex, Schizophrenia			disease		Uni-ZAP XR
S0051	Human Hypothalamus, Schizophrenia	Human Hypothalamus, Schizophrenia			disease		Uni-ZAP XR
S0052	neutrophils control	human neutrophils	blood		Cell Line		Uni-ZAP XR
S0053	Neutrophils IL-1 and LPS induced	human neutrophil induced	blood		Cell Line		Uni-ZAP XR
S0106	STRIATUM DEPRESSION		BRAIN		disease		Uni-ZAP XR
S0110	Brain Amygdala Depression		Brain		disease		Uni-ZAP XR
S0112	Hypothalamus		Brain				Uni-ZAP XR
S0114	Anergic T-cell	Anergic T-cell			Cell Line		Uni-ZAP XR
S0116	Bone marrow	Bone marrow	Bone marrow				Uni-ZAP XR
S0122	Osteoclastoma-normalized A	Osteoclastoma	bone		disease		pBluescript
S0124	Smooth muscle-edited A	Smooth muscle	Pulmonary artery		Cell Line		Uni-ZAP XR
S0126	Osteoblasts	Osteoblasts	Knee		Cell Line		Uni-ZAP XR
S0132	Epithelial-TNF α and INF induced	Airway Epithelial					Uni-ZAP XR
S0134	Apoptotic T-cell	apoptotic cells			Cell Line		Uni-ZAP XR
S0136	PERM TF274	stromal cell	Bone marrow		Cell Line		Lambda ZAP II
S0140	eosinophil-IL5 induced	eosinophil	lung		Cell Line		Uni-ZAP XR
S0142	Macrophage-oxLDL	macrophage-oxidized LDL treated	blood		Cell Line		Uni-ZAP XR
S0144	Macrophage (GM-CSF treated)	Macrophage (GM-CSF treated)					Uni-ZAP XR
S0146	prostate-edited	prostate BPH	Prostate				Uni-ZAP XR
S0148	Normal Prostate	Prostate	prostate				Uni-ZAP XR
S0150	LNCAP prostate cell line	LNCAP Cell Line	Prostate		Cell Line		Uni-ZAP XR
S0152	PC3 Prostate cell line	PC3 prostate cell line					Uni-ZAP XR

S0168	Prostate/LNCAP, subtraction I	PC3 prostate cell line				pBluescript
S0176	Prostate, normal, subtraction I	Prostate	prostate			Uni-ZAP XR
S0180	Bone Marrow Stroma, TNF&LPS ind	Bone Marrow Stroma, TNF & LPS induced			disease	Uni-ZAP XR
S0182	Human B Cell 8866	Human B- Cell 8866				Uni-ZAP XR
S0188	Prostate, BPH, Lib 2	Human Prostate BPH			disease	pSport1
S0190	Prostate BPH, Lib 2, subtracted	Human Prostate BPH				pSport1
S0192	Synovial Fibroblasts (control)	Synovial Fibroblasts				pSport1
S0194	Synovial hypoxia	Synovial Fibroblasts				pSport1
S0196	Synovial IL-1/TNF stimulated	Synovial Fibroblasts				pSport1
S0206	Smooth Muscle- HASTE normalized	Smooth muscle	Pulmonary artery	Cell Line		pBluescript
S0208	Mesangial cell, frac 1	Mesangial cell				pSport1
S0210	Mesangial cell, frac 2	Mesangial cell				pSport1
S0212	Bone Marrow Stromal Cell, untreated	Bone Marrow Stromal Cell, untreated				pSport1
S0214	Human Osteoclastoma, re-excision	Osteoclastoma	bone		disease	Uni-ZAP XR
S0216	Neutrophils IL-1 and LPS induced	human neutrophil induced	blood	Cell Line		Uni-ZAP XR
S0218	Apoptotic T-cell, re-excision	apoptotic cells		Cell Line		Uni-ZAP XR
S0220	H. hypothalamus, frac A; re-excision	Hypothalamus	Brain			ZAP Express
S0222	H. Frontal cortex, epileptic; re-excision	H. Brain, Frontal Cortex, Epileptic	Brain		disease	Uni-ZAP XR
S0242	Synovial Fibroblasts	Synovial Fibroblasts				pSport1

	(Il1/TNF), subt							
S0250	Human Osteoblasts II	Human Osteoblasts	Femur			disease		pCMVSPORT 2.0
S0260	Spinal Cord, re-excision	Spinal cord	spinal cord					Uni-ZAP XR
S0276	Synovial hypoxia-RSF subtracted	Synovial fobroblasts (rheumatoid)	Synovial tissue					pSport1
S0278	H Macrophage (GM-CSF treated), re-excision	Macrophage (GM-CSF treated)						Uni-ZAP XR
S0280	Human Adipose Tissue, re-excision	Human Adipose Tissue						Uni-ZAP XR
S0282	Brain Frontal Cortex, re-excision	Brain frontal cortex	Brain					Lambda ZAP II
S0292	Osteoarthritis (OA-4)	Human Osteoarthritic Cartilage	Bone			disease		pSport1
S0294	Larynx tumor	Larynx tumor	Larynx, vocal cord			disease		pSport1
S0298	Bone marrow stroma, treated	Bone marrow stroma, treated SB	Bone marrow					pSport1
S0300	Frontal lobe, dementia; re-excision	Frontal Lobe dementia/Alzheimer's	Brain					Uni-ZAP XR
S0306	Larynx normal #10 261-273	Larynx normal						pSport1
S0308	Spleen/normal	Spleen normal						pSport1
S0310	Normal trachea	Normal trachea						pSport1
S0312	Human osteoarthritic; fraction II	Human osteoarthritic cartilage				disease		pSport1
S0314	Human osteoarthritic; fraction I	Human osteoarthritic cartilage				disease		pSport1
S0316	Human Normal Cartilage, Fraction I	Human Normal Cartilage						pSport1
S0318	Human Normal Cartilage Fraction II	Human Normal Cartilage						pSport1
S0328	Palate carcinoma	Palate carcinoma	Uvula			disease		pSport1
S0330	Palate normal	Palate normal	Uvula					pSport1
S0332	Pharynx carcinoma	Pharynx carcinoma	Hypopharynx					pSport1

S0334	Human Normal Cartilage Fraction III	Human Normal Cartilage				pSport1
S0336	Human Normal Cartilage Fraction IV	Human Normal Cartilage				pSport1
S0338	Human Osteoarthritic Cartilage Fraction III	Human osteoarthritic cartilage			disease	pSport1
S0340	Human Osteoarthritic Cartilage Fraction IV	Human osteoarthritic cartilage			disease	pSport1
S0342	Adipocytes;re-excision	Human Adipocytes from Osteoclastoma				Uni-ZAP XR
S0344	Macrophage-oxLDL; re-excision	macrophage-oxidized LDL treated	blood	Cell Line		Uni-ZAP XR
S0346	Human Amygdala;re-excision	Amygdala				Uni-ZAP XR
S0348	Cheek Carcinoma	Cheek Carcinoma			disease	pSport1
S0350	Pharynx Carcinoma	Pharynx carcinoma	Hypopharynx		disease	pSport1
S0352	Larynx Carcinoma	Larynx carcinoma			disease	pSport1
S0354	Colon Normal II	Colon Normal	Colon			pSport1
S0356	Colon Carcinoma	Colon Carcinoma	Colon		disease	pSport1
S0358	Colon Normal III	Colon Normal	Colon			pSport1
S0360	Colon Tumor II	Colon Tumor	Colon		disease	pSport1
S0362	Human Gastrocnemius	Gastrocnemius muscle				pSport1
S0364	Human Quadriceps	Quadriceps muscle				pSport1
S0366	Human Soleus	Soleus Muscle				pSport1
S0368	Human Pancreatic Langerhans	Islets of Langerhans				pSport1
S0370	Larynx carcinoma II	Larynx carcinoma			disease	pSport1
S0372	Larynx carcinoma III	Larynx carcinoma			disease	pSport1
S0374	Normal colon	Normal colon				pSport1
S0376	Colon Tumor	Colon Tumor			disease	pSport1
S0378	Pancreas normal PCA4 No	Pancreas Normal PCA4 No				pSport1
S0380	Pancreas Tumor PCA4	Pancreas Tumor PCA4 Tu			disease	pSport1

	Tu							
S0382	Larynx carcinoma IV	Larynx carcinoma					disease	pSport1
S0384	Tongue carcinoma	Tongue carcinoma					disease	pSport1
S0386	Human Whole Brain, re-excision	Whole brain	Brain					ZAP Express
S0388	Human Hypothalamus, schizophr enia, re-excision	Human Hypothalamus, Schizophrenia					disease	Uni-ZAP XR
S0390	Smooth muscle, control; re-excision	Smooth muscle	Pulmonary artery			Cell Line		Uni-ZAP XR
S0392	Salivary Gland	Salivary gland; normal						pSport1
S0394	Stomach; normal	Stomach; normal						pSport1
S0398	Testis; normal	Testis; normal						pSport1
S0400	Brain; normal	Brain; normal						pSport1
S0402	Adrenal Gland; normal	Adrenal gland; normal						pSport1
S0404	Rectum normal	Rectum; normal						pSport1
S0406	Rectum tumour	Rectum tumour						pSport1
S0408	Colon, normal	Colon, normal						pSport1
S0410	Colon, tumour	Colon, tumour						pSport1
S0412	Temporal cortex- Alzheimer; subtracted	Temporal cortex, alzheimer					disease	Other
S0414	Hippocampus, Alzheimer Subtracted	Hippocampus, Alzheimer Subtracted						Other
S0418	CHME Cell Line; treated 5 hrs	CHME Cell Line; treated						pCMV/Sport 3.0
S0420	CHME Cell Line, untreated	CHME Cell line, untreated						pSport1
S0422	Mo7e Cell Line GM-CSF treated (1ng/ml)	Mo7e Cell Line GM-CSF treated (1ng/ml)						pCMV/Sport 3.0
S0424	TF-1 Cell Line GM-CSF Treated	TF-1 Cell Line GM-CSF Treated						pSport1
S0426	Monocyte activated; re-excision	Monocyte-activated	blood			Cell Line		Uni-ZAP XR

S0428	Neutrophils control; re-excision	human neutrophils	blood	Cell Line	Uni-ZAP XR
S0430	Aryepiglottis Normal	Aryepiglottis Normal			pSport1
S0432	Sinus piniformis Tumour	Sinus piniformis Tumour			pSport1
S0434	Stomach Normal	Stomach Normal		disease	pSport1
S0436	Stomach Tumour	Stomach Tumour		disease	pSport1
S0438	Liver Normal Met5No	Liver Normal Met5No			pSport1
S0440	Liver Tumour Met 5 Tu	Liver Tumour			pSport1
S0442	Colon Normal	Colon Normal			pSport1
S0444	Colon Tumour	Colon Tumour		disease	pSport1
S0446	Tongue Tumour	Tongue Tumour			pSport1
S0448	Larynx Normal	Larynx Normal			pSport1
S0450	Larynx Tumour	Larynx Tumour			pSport1
S0452	Thymus	Thymus			pSport1
S0454	Placenta	Placenta	Placenta		pSport1
S0456	Tongue Normal	Tongue Normal			pSport1
S0458	Thyroid Normal (SDCA2 No)	Thyroid normal			pSport1
S0460	Thyroid Tumour	Thyroid Tumour			pSport1
S0462	Thyroid Thyroiditis	Thyroid Thyroiditis			pSport1
S0464	Larynx Normal	Larynx Normal			pSport1
S0466	Larynx Tumour	Larynx Tumour		disease	pSport1
S0468	Ea.hy.926 cell line	Ea.hy.926 cell line			pSport1
S0470	Adenocarcinoma	PYFD		disease	pSport1
S0472	Lung Mesothelium	PYBT			pSport1
S0474	Human blood platelets	Platelets	Blood platelets		Other
S0665	Human Amygdala; re-excision	Amygdala			Uni-ZAP XR
S3012	Smooth Muscle Serum Treated, Norm	Smooth muscle	Pulmonary artery	Cell Line	pBluescript
S3014	Smooth muscle, serum induced, re-exc	Smooth muscle	Pulmonary artery	Cell Line	pBluescript

S6014	H. hypothalamus, frac A	Hypothalamus	Brain			ZAP Express
S6016	H. Frontal Cortex, Epileptic	H. Brain, Frontal Cortex, Epileptic	Brain		disease	Uni-ZAP XR
S6022	H. Adipose Tissue	Human Adipose Tissue				Uni-ZAP XR
S6024	Alzheimer's, spongy change	Alzheimer's/Spongy change	Brain		disease	Uni-ZAP XR
S6026	Frontal Lobe, Dementia	Frontal Lobe dementia/Alzheimer's	Brain			Uni-ZAP XR
S6028	Human Manic Depression Tissue	Human Manic depression tissue	Brain		disease	Uni-ZAP XR
T0002	Activated T-cells	Activated T-Cell, PBL fraction	Blood	Cell Line		pBluescript SK-
T0003	Human Fetal Lung	Human Fetal Lung				pBluescript SK-
T0004	Human White Fat	Human White Fat				pBluescript SK-
T0006	Human Pineal Gland	Human Pineal Gland				pBluescript SK-
T0007	Colon Epithelium	Colon Epithelium				pBluescript SK-
T0008	Colorectal Tumor	Colorectal Tumor			disease	pBluescript SK-
T0010	Human Infant Brain	Human Infant Brain				Other
T0023	Human Pancreatic Carcinoma	Human Pancreatic Carcinoma			disease	pBluescript SK-
T0039	HSA 172 Cells	Human HSA172 cell line				pBluescript SK-
T0040	HSC172 cells	SA172 Cells				pBluescript SK-
T0041	Jurkat T-cell G1 phase	Jurkat T-cell				pBluescript SK-
T0042	Jurkat T-Cell, S phase	Jurkat T-Cell Line				pBluescript SK-
T0048	Human Aortic Endothelium	Human Aortic Endothelium				pBluescript SK-
T0049	Aorta endothelial cells + TNF-a	Aorta endothelial cells				pBluescript SK-
T0060	Human White Adipose	Human White Fat				pBluescript SK-
T0067	Human Thyroid	Human Thyroid				pBluescript SK-
T0068	Normal Ovary, Premenopausal	Normal Ovary, Premenopausal				pBluescript SK-
T0069	Human Uterus, normal	Human Uterus, normal				pBluescript SK-

T0071	Human Bone Marrow	Human Bone Marrow					pBluescript SK-
T0079	Human Kidney, normal Adult	Human Kidney, normal Adult					pBluescript SK-
T0082	Human Adult Retina	Human Adult Retina					pBluescript SK-
T0086	Human Pancreatic Carcinoma -- Screened	Human Pancreatic Carcinoma				disease	pBluescript SK-
T0087	Alzheimer's, exon trap, 712P					disease	pAMP
T0103	Human colon carcinoma (HCC) cell line						pBluescript SK-
T0104	HCC cell line metastasis to liver						pBluescript SK-
T0109	Human (HCC) cell line liver (mouse) metastasis, remake						pBluescript SK-
T0110	Human colon carcinoma (HCC) cell line, remake						pBluescript SK-
T0112	Human (Caco-2) cell line, adenocarcinoma, colon						pBluescript SK-
T0114	Human (Caco-2) cell line, adenocarcinoma, colon, remake						pBluescript SK-
T0115	Human Colon Carcinoma (HCC) cell line						pBluescript SK-
L0002	Atrium cDNA library Human heart						
L0005	Clontech human aorta polyA+ mRNA (#6572)						
L0015	Human						
L0021	Human adult (K.Okubo)						
L0022	Human adult lung 3" directed Mbol cDNA						

L0024	Human brain ARSanders								
L0040	Human colon mucosa								
L0041	Human epidermal keratinocyte								
L0045	Human keratinocyte differential display (B.Lin)								
L0053	Human pancreatic tumor								
L0055	Human promyelocyte								
L0065	Liver HepG2 cell line.								
L0096	Subtracted human retina								
L0097	Subtracted human retinal pigment epithelium (RPE)								
L0103	DKFZphamy1					amygdala			
L0105	Human aorta polyA+ (TFujiwara)					aorta			
L0142	Human placenta cDNA (TFujiwara)					placenta			
L0143	Human placenta polyA+ (TFujiwara)					placenta			
L0151	Human testis (C. De Smet)					testis			
L0157	Human fetal brain (TFujiwara)						brain		
L0163	Human heart cDNA (YNakamura)						heart		
L0182	Human HeLa (Y.Wang)							HeLa	
L0187	Human fibrosarcoma cell line HT1080					fibrosarcoma		HT1080	
L0194	Human pancreatic cancer cell line Patu 8988t					pancreatic cancer		Patu 8988t	
L0295	Human liver EST						liver		

	(Y.L. Yu)	breast adenocarcinoma		E8CASS; variant of MCF7		
L0309	Human E8CASS	breast adenocarcinoma				
L0351	Infant brain, Bento Soares					BA, M13-derived
L0352	Normalized infant brain, Bento Soares					BA, M13-derived
L0355	P, Human foetal Brain Whole tissue					Bluescript
L0356	S, Human foetal Adrenals tissue					Bluescript
L0361	Stratagene ovary (#937217)	ovary				Bluescript SK
L0362	Stratagene ovarian cancer (#937219)					Bluescript SK-
L0363	NCL_CGAP_GC2	germ cell tumor				Bluescript SK-
L0364	NCL_CGAP_GC5	germ cell tumor				Bluescript SK-
L0365	NCL_CGAP_Phe1	pheochromocytoma				Bluescript SK-
L0366	Stratagene schizo brain S11	schizophrenic brain S-11 frontal lobe				Bluescript SK-
L0367	NCL_CGAP_Sch1	Schwannoma tumor				Bluescript SK-
L0368	NCL_CGAP_SS1	synovial sarcoma				Bluescript SK-
L0369	NCL_CGAP_AA1	adrenal adenoma	adrenal gland			Bluescript SK-
L0370	Johnston frontal cortex	pooled frontal lobe	brain			Bluescript SK-
L0371	NCL_CGAP_Br3	breast tumor	breast			Bluescript SK-
L0372	NCL_CGAP_Col2	colon tumor	colon			Bluescript SK-
L0373	NCL_CGAP_Col1	tumor	colon			Bluescript SK-
L0374	NCL_CGAP_Co2	tumor	colon			Bluescript SK-
L0375	NCL_CGAP_Kid6	kidney tumor	kidney			Bluescript SK-
L0376	NCL_CGAP_Lar1	larynx	larynx			Bluescript SK-
L0378	NCL_CGAP_Lu1	lung tumor	lung			Bluescript SK-
L0379	NCL_CGAP_Lym3	lymphoma	lymph node			Bluescript SK-

L0381	NCL_CGAP_HN4	squamous cell carcinoma	pharynx		Bluescript SK-
L0382	NCL_CGAP_Pr25	epithelium (cell line)	prostate		Bluescript SK-
L0383	NCL_CGAP_Pr24	invasive tumor (cell line)	prostate		Bluescript SK-
L0384	NCL_CGAP_Pr23	prostate tumor	prostate		Bluescript SK-
L0385	NCL_CGAP_Gas1	gastric tumor	stomach		Bluescript SK-
L0386	NCL_CGAP_HN3	squamous cell carcinoma from base of tongue	tongue		Bluescript SK-
L0387	NCL_CGAP_GCB0	germinal center B-cells	tonsil		Bluescript SK-
L0388	NCL_CGAP_HN6	normal gingiva (cell line from immortalized kerati			Bluescript SK-
L0389	NCL_CGAP_HN5	normal gingiva (cell line from primary keratinocyt			Bluescript SK-
L0394	H, Human adult Brain Cortex tissue				gt11
L0404	b4HB3MA Cot109+103+85-Bio				Lafmid A
L0411	l-NIB				Lafmid BA
L0415	b4HB3MA Cot8-HAP-Ft				Lafmid BA
L0418	b4HB3MA-Cot109+10-Bio				Lafmid BA
L0428	Cot1374Fr-4HB3MA				Lafmid BA
L0435	Infant brain, LLNL array of Dr. M. Soares INIB				lafmid BA
L0438	normalized infant brain cDNA	total brain	brain		lafmid BA
L0439	Soares infant brain INIB		whole brain		Lafmid BA
L0446	N4HB3MK				Lafmid BK
L0455	Human retina cDNA randomly primed sublibrary	retina	eye		lambda gt10
L0456	Human retina cDNA Tsp509I-cleaved sublibrary	retina	eye		lambda gt10

L0457	multi-tissue normalized short-fragment	multi-tissue	pooled			lambda gt10
L0459	Adult heart, Clontech					Lambda gt11
L0460	Adult heart, Lambda gt11					Lambda gt11
L0462	WATM1					lambda gt11
L0463	fetal brain cDNA	brain	brain			lambda gt11
L0465	TEST1, Human adult Testis tissue					lambda nm1149
L0471	Human fetal heart, Lambda ZAP Express					Lambda ZAP Express
L0475	KG1-a Lambda Zap Express cDNA library			KG1-a		Lambda Zap Express (Stratagene)
L0476	Fetal brain, Stratagene					Lambda ZAP II
L0480	Stratagene cat#937212 (1992)					Lambda ZAP, pBluescript SK(-)
L0481	CD34+DIRECTIONAL					Lambda ZAPII
L0483	Human pancreatic islet					Lambda ZAPII
L0485	STRATAGENE Human skeletal muscle cDNA library, cat. #936215.	skeletal muscle	leg muscle			Lambda ZAPII
L0492	Human Genomic					
L0493	NCL_CGAP_Ov26	papillary serous carcinoma	ovary			pAMP
L0497	NCL_CGAP_HSC4	CD34+, CD38- from normal bone marrow donor	bone marrow			pAMP1
L0498	NCL_CGAP_HSC3	CD34+, T negative, patient with chronic myelogenous	bone marrow			pAMP1
L0499	NCL_CGAP_HSC2	stem cell 34+/38+	bone marrow			pAMP1
L0500	NCL_CGAP_Bm20	oligodendrogloma	brain			pAMP1
L0502	NCL_CGAP_Br15	adenocarcinoma	breast			pAMP1
L0503	NCL_CGAP_Br17	adenocarcinoma	breast			pAMP1

L0504	NCL_CGAP_Br13	breast carcinoma in situ	breast			pAMP1
L0505	NCL_CGAP_Br12	invasive carcinoma	breast			pAMP1
L0506	NCL_CGAP_Br16	lobular carcinoma in situ	breast			pAMP1
L0507	NCL_CGAP_Br14	normal epithelium	breast			pAMP1
L0508	NCL_CGAP_Lu25	bronchioalveolar carcinoma	lung			pAMP1
L0509	NCL_CGAP_Lu26	invasive adenocarcinoma	lung			pAMP1
L0512	NCL_CGAP_Ov36	borderline ovarian carcinoma	ovary			pAMP1
L0513	NCL_CGAP_Ov37	early stage papillary serous carcinoma	ovary			pAMP1
L0514	NCL_CGAP_Ov31	papillary serous carcinoma	ovary			pAMP1
L0515	NCL_CGAP_Ov32	papillary serous carcinoma	ovary			pAMP1
L0517	NCL_CGAP_Pr1					pAMP10
L0518	NCL_CGAP_Pr2					pAMP10
L0519	NCL_CGAP_Pr3					pAMP10
L0520	NCL_CGAP_Alv1	alveolar rhabdomyosarcoma				pAMP10
L0521	NCL_CGAP_Ew1	Ewing's sarcoma				pAMP10
L0522	NCL_CGAP_Kid1	kidney				pAMP10
L0523	NCL_CGAP_Lip2	liposarcoma				pAMP10
L0524	NCL_CGAP_Li1	liver				pAMP10
L0525	NCL_CGAP_Li2	liver				pAMP10
L0526	NCL_CGAP_Pr12	metastatic prostate bone lesion				pAMP10
L0527	NCL_CGAP_Ov2	ovary				pAMP10
L0528	NCL_CGAP_Pr5	prostate				pAMP10
L0529	NCL_CGAP_Pr6	prostate				pAMP10
L0530	NCL_CGAP_Pr8	prostate				pAMP10
L0532	NCL_CGAP_Thy1	thyroid				pAMP10
L0533	NCL_CGAP_HSC1	stem cells	bone marrow			pAMP10
L0534	Chromosome 7 Fetal	brain	brain			pAMP10

L0539	Brain cDNA Library			placenta			pAMP10
L0540	Chromosome 7 Placental cDNA Library						pAMP10
L0542	NCL_CGAP_Pr10	invasive prostate tumor		prostate			pAMP10
L0543	NCL_CGAP_Pr11	normal prostatic epithelial cells		prostate			pAMP10
L0544	NCL_CGAP_Pr9	normal prostatic epithelial cells		prostate			pAMP10
L0545	NCL_CGAP_Pr4	prostatic intraepithelial neoplasia - high grade		prostate			pAMP10
L0546	NCL_CGAP_Pr4.1	prostatic intraepithelial neoplasia - high grade		prostate			pAMP10
L0547	NCL_CGAP_Pr18	stroma		prostate			pAMP10
L0548	NCL_CGAP_Pr16	tumor		prostate			pAMP10
L0549	NCL_CGAP_HN10	carcinoma in situ from retromolar trigone					pAMP10
L0550	NCL_CGAP_HN9	normal squamous epithelium from retromolar trigone					pAMP10
L0551	NCL_CGAP_HN7	normal squamous epithelium, floor of mouth					pAMP10
L0552	NCL_CGAP_Co22	colonic adenocarcinoma		colon			pAMP10
L0553	NCL_CGAP_Li8			liver			pAMP10
L0554	NCL_CGAP_Ov40	endometrioid ovarian metastasis		ovary			pAMP10
L0555	NCL_CGAP_Ov39	papillary serous ovarian metastasis		ovary			pAMP10
L0556	NCL_CGAP_HN12	moderate to poorly differentiated invasive carcino		tongue			pAMP10
L0557	NCL_CGAP_HN11	normal squamous epithelium		tongue			pAMP10
L0558	Chromosome 7 HeLa				HeLa cell line;		pAMP10

	cDNA Library			ATCC		
L0564	Jia bone marrow stroma					pBluescript
L0565	Normal Human					pBluescript
	Trabecular Bone Cells		Hip			
L0581	Stratagene liver (#937224)		liver			pBluescript SK
L0584	Stratagene cDNA library Human heart, cat#936208					pBluescript SK(+)
L0586	HTC DLI					pBluescript SK(-)
L0587	Stratagene colon HT29 (#937221)					pBluescript SK-
L0588	Stratagene endothelial cell 937223					pBluescript SK-
L0589	Stratagene fetal retina 937202					pBluescript SK-
L0590	Stratagene fibroblast (#937212)					pBluescript SK-
L0591	Stratagene HeLa cell s3 937216					pBluescript SK-
L0592	Stratagene hNT neuron (#937233)					pBluescript SK-
L0593	Stratagene neuroepithelium (#937231)					pBluescript SK-
L0594	Stratagene neuroepithelium NT2RAMI 937234					pBluescript SK-
L0595	Stratagene NT2 neuronal precursor 937230		brain			pBluescript SK-
L0596	Stratagene colon (#937204)		colon			pBluescript SK-
L0597	Stratagene corneal		cornea			pBluescript SK-

	stroma (#937222)								
L0598	Morton Fetal Cochlea	cochlea	ear					pBluescript SK-	
L0599	Stratagene lung (#937210)		lung					pBluescript SK-	
L0600	Weizmann Olfactory Epithelium	olfactory epithelium	nose					pBluescript SK-	
L0601	Stratagene pancreas (#937208)		pancreas					pBluescript SK-	
L0602	Pancreatic Islet	pancreatic islet	pancreas					pBluescript SK-	
L0603	Stratagene placenta (#937225)		placenta					pBluescript SK-	
L0604	Stratagene muscle 937209	muscle	skeletal muscle					pBluescript SK-	
L0605	Stratagene fetal spleen (#937205)	fetal spleen	spleen					pBluescript SK-	
L0606	NCI CGAP Lym5	follicular lymphoma	lymph node					pBluescript SK-	
L0607	NCI CGAP Lym6	mantle cell lymphoma	lymph node					pBluescript SK-	
L0608	Stratagene lung carcinoma 937218	lung carcinoma	lung			NCI-H69		pBluescript SK-	
L0609	Schiller astrocytoma	astrocytoma	brain					pBluescript SK- (Stratagene)	
L0610	Schiller glioblastoma multiforme	glioblastoma multiforme	brain					pBluescript SK- (Stratagene)	
L0611	Schiller meningioma	meningioma	brain					pBluescript SK- (Stratagene)	
L0612	Schiller oligodendroglioma	oligodendroglioma	brain					pBluescript SK- (Stratagene)	
L0615	22 week old human fetal liver cDNA library							pBluescript SK- (Stratagene)	
L0619	Chromosome 9 exon II							pBluescript SK- (-)	
L0622	HM1							pBluescript SK- (+)	
L0623	HM3	pectoral muscle (after mastectomy)						pcDNAII (Invitrogen)	

L0625	NCI_CGAP_AR1	bulk alveolar tumor				pCMV-SPORT2
L0626	NCI_CGAP_GC1	bulk germ cell seminoma				pCMV-SPORT2
L0627	NCI_CGAP_Co1	bulk tumor	colon			pCMV-SPORT2
L0628	NCI_CGAP_Ov1	ovary bulk tumor	ovary			pCMV-SPORT2
L0629	NCI_CGAP_Mel3	metastatic melanoma to bowel	bowel (skin primary)			pCMV-SPORT4
L0630	NCI_CGAP_CNS1	substantia nigra	brain			pCMV-SPORT4
L0631	NCI_CGAP_Br7		breast			pCMV-SPORT4
L0634	NCI_CGAP_Ov8	serous adenocarcinoma	ovary			pCMV-SPORT4
L0635	NCI_CGAP_PNS1	dorsal root ganglion	peripheral nervous system			pCMV-SPORT4
L0636	NCI_CGAP_Pit1	four pooled pituitary adenomas	brain			pCMV-SPORT6
L0637	NCI_CGAP_Bm53	three pooled meningiomas	brain			pCMV-SPORT6
L0638	NCI_CGAP_Bm35	tumor, 5 pooled (see description)	brain			pCMV-SPORT6
L0639	NCI_CGAP_Bm52	tumor, 5 pooled (see description)	brain			pCMV-SPORT6
L0640	NCI_CGAP_Br18	four pooled high-grade tumors, including two prima	breast			pCMV-SPORT6
L0641	NCI_CGAP_Co17	juvenile granulosa tumor	colon			pCMV-SPORT6
L0642	NCI_CGAP_Co18	moderately differentiated adenocarcinoma	colon			pCMV-SPORT6
L0643	NCI_CGAP_Co19	moderately differentiated adenocarcinoma	colon			pCMV-SPORT6
L0644	NCI_CGAP_Co20	moderately differentiated adenocarcinoma	colon			pCMV-SPORT6
L0645	NCI_CGAP_Co21	moderately differentiated adenocarcinoma	colon			pCMV-SPORT6
L0646	NCI_CGAP_Co14	moderately-differentiated adenocarcinoma	colon			pCMV-SPORT6
L0647	NCI_CGAP_Sar4	five pooled sarcomas,	connective tissue			pCMV-SPORT6

			including myxoid liposarcoma					
L0648	NCI_CGAP_Eso2		squamous cell carcinoma	esophagus				pCMV-SPORT6
L0649	NCI_CGAP_GU1		2 pooled high-grade transitional cell tumors	genitourinary tract				pCMV-SPORT6
L0650	NCI_CGAP_Kid13		2 pooled Wilms' tumors, one primary and one metast	kidney				pCMV-SPORT6
L0651	NCI_CGAP_Kid8		renal cell tumor	kidney				pCMV-SPORT6
L0652	NCI_CGAP_Lu27		four pooled poorly-differentiated adenocarcinomas	lung				pCMV-SPORT6
L0653	NCI_CGAP_Lu28		two pooled squamous cell carcinomas	lung				pCMV-SPORT6
L0654	NCI_CGAP_Lu31			lung, cell line				pCMV-SPORT6
L0655	NCI_CGAP_Lym12		lymphoma, follicular mixed small and large cell	lymph node				pCMV-SPORT6
L0656	NCI_CGAP_Ov38		normal epithelium	ovary				pCMV-SPORT6
L0657	NCI_CGAP_Ov23		tumor, 5 pooled (see description)	ovary				pCMV-SPORT6
L0658	NCI_CGAP_Ov35		tumor, 5 pooled (see description)	ovary				pCMV-SPORT6
L0659	NCI_CGAP_Pan1		adenocarcinoma	pancreas				pCMV-SPORT6
L0661	NCI_CGAP_Mel15		malignant melanoma, metastatic to lymph node	skin				pCMV-SPORT6
L0662	NCI_CGAP_Gas4		poorly differentiated adenocarcinoma with signet r	stomach				pCMV-SPORT6
L0663	NCI_CGAP_Ut2		moderately-differentiated endometrial adenocarcinoma	uterus				pCMV-SPORT6
L0664	NCI_CGAP_Ut3		poorly-differentiated endometrial adenocarcinoma,	uterus				pCMV-SPORT6

L0665	NCL_CGAP_Ut4	serous papillary carcinoma, high grade, 2 pooled t	uterus			pCMV-SPORT6
L0666	NCL_CGAP_Ut1	well-differentiated endometrial adenocarcinoma, 7	uterus			pCMV-SPORT6
L0667	NCL_CGAP_CML1	myeloid cells, 18 pooled CML cases, BCR/ABL reara	whole blood			pCMV-SPORT6
L0686	Stanley Frontal SN pool 2	frontal lobe (see description)	brain			pCR2.1-TOPO (Invitrogen)
L0690	Testis, Subtracted					pCRII
L0697	Testis 1					PGEM 5zf(+)
L0698	Testis 2					PGEM 5zf(+)
L0708	NIH_MGC_17	rhabdomyosarcoma	muscle			POTB7
L0709	NIH_MGC_21	choriocarcinoma	placenta			POTB7
L0710	NIH_MGC_7	small cell carcinoma	lung	MGC3		POTB7
L0717	Gessler Wilms tumor					pSPORT1
L0731	Soares_pregnant_uterus_NbHPU		uterus			pT7T3-Pac
L0738	Human colorectal cancer					pT7T3D
L0740	Soares melanocyte 2NbHM	melanocyte				pT7T3D (Pharmacia) with a modified polylinker
L0741	Soares adult brain N2b4HB55Y		brain			pT7T3D (Pharmacia) with a modified polylinker
L0742	Soares adult brain N2b5HB55Y		brain			pT7T3D (Pharmacia) with a modified polylinker
L0743	Soares breast 2NbHBst		breast			pT7T3D (Pharmacia) with a modified polylinker

L0744	Soares breast 3NbHBst		breast			pT7T3D (Pharmacia) with a modified polylinker
L0745	Soares retina N2b4HR	retina	eye			pT7T3D (Pharmacia) with a modified polylinker
L0746	Soares retina N2b5HR	retina	eye			pT7T3D (Pharmacia) with a modified polylinker
L0747	Soares_fetal_heart_NbH H19W		heart			pT7T3D (Pharmacia) with a modified polylinker
L0748	Soares fetal liver spleen 1NFLS		Liver and Spleen			pT7T3D (Pharmacia) with a modified polylinker
L0749	Soares_fetal_liver_splee n_1NFLS_S1		Liver and Spleen			pT7T3D (Pharmacia) with a modified polylinker
L0750	Soares_fetal_lung_NbHL 19W		lung			pT7T3D (Pharmacia) with a modified polylinker
L0751	Soares ovary tumor NbHOT	ovarian tumor	ovary			pT7T3D (Pharmacia) with a modified polylinker
L0752	Soares_parathyroid_tum or_NbHPA	parathyroid tumor	parathyroid gland			pT7T3D (Pharmacia) with a modified polylinker
L0753	Soares_pineal_gland_N3 HPG		pineal gland			pT7T3D (Pharmacia) with a modified polylinker
L0754	Soares placenta Nb2HP		placenta			pT7T3D (Pharmacia) with a modified polylinker

L0755	Soares_placenta_8to9weeks_2NbHP8to9W		placenta			pT7T3D (Pharmacia) with a modified polylinker
L0756	Soares_multiple_sclerosiss_2NbHMSP	multiple sclerosis lesions				pT7T3D (Pharmacia) with a modified polylinker V_TYPE
L0757	Soares_senescent_fibroblasts_NbHSF	senescent fibroblast				pT7T3D (Pharmacia) with a modified polylinker V_TYPE
L0758	Soares_testis_NHT					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0759	Soares_total_fetus_Nb2HF8_9w					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0760	Barstead aorta HPLRB3	aorta				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0761	NCL_CGAP_CLL1	B-cell, chronic lymphocytic leukemia				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0762	NCL_CGAP_Br1.1	breast				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0763	NCL_CGAP_Br2	breast				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0764	NCL_CGAP_Co3	colon				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0765	NCL_CGAP_Co4	colon				pT7T3D-Pac (Pharmacia) with a modified polylinker

L0766	NCI_CGAP_GCB1	germinal center B cell				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0767	NCI_CGAP_GC3	pooled germ cell tumors				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0768	NCI_CGAP_GC4	pooled germ cell tumors				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0769	NCI_CGAP_Bm25	anaplastic oligodendroglioma	brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0770	NCI_CGAP_Bm23	glioblastoma (pooled)	brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0771	NCI_CGAP_Co8	adenocarcinoma	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0772	NCI_CGAP_Co10	colon tumor RER+	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0773	NCI_CGAP_Co9	colon tumor RER+	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0774	NCI_CGAP_Kid3		kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0775	NCI_CGAP_Kid5	2 pooled tumors (clear cell type)	kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0776	NCI_CGAP_Lu5	carcinoid	lung			pT7T3D-Pac (Pharmacia) with a modified polylinker

L0777	Soares_NhHMPu_S1	Pooled human melanocyte, fetal heart, and pregnant	mixed (see below)			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0778	Barstead pancreas HPLRB1		pancreas			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0779	Soares_NFL_T_GBC_S1		pooled			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0780	Soares_NSF_F8_9W_O T_PA_P_S1		pooled			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0782	NCL_CGAP_Pr21	normal prostate	prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0783	NCL_CGAP_Pr22	normal prostate	prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0784	NCL_CGAP_Lei2	leiomyosarcoma	soft tissue			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0785	Barstead spleen HPLRB2		spleen			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0786	Soares_NbHFB		whole brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0787	NCL_CGAP_Sub1					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0788	NCL_CGAP_Sub2					pT7T3D-Pac (Pharmacia) with a modified polylinker

L0789	NCL_CGAP_Sub3						pT7T3D-Pac (Pharmacia) with a modified polylinker
L0790	NCL_CGAP_Sub4						pT7T3D-Pac (Pharmacia) with a modified polylinker
L0791	NCL_CGAP_Sub5						pT7T3D-Pac (Pharmacia) with a modified polylinker
L0792	NCL_CGAP_Sub6						pT7T3D-Pac (Pharmacia) with a modified polylinker
L0793	NCL_CGAP_Sub7						pT7T3D-Pac (Pharmacia) with a modified polylinker
L0794	NCL_CGAP_GC6				pooled germ cell tumors		pT7T3D-Pac (Pharmacia) with a modified polylinker
L0796	NCL_CGAP_Brm50				medulloblastoma	brain	pT7T3D-Pac (Pharmacia) with a modified polylinker
L0800	NCL_CGAP_Co16				colon tumor, RER+	colon	pT7T3D-Pac (Pharmacia) with a modified polylinker
L0803	NCL_CGAP_Kid11					kidney	pT7T3D-Pac (Pharmacia) with a modified polylinker
L0804	NCL_CGAP_Kid12				2 pooled tumors (clear cell type)	kidney	pT7T3D-Pac (Pharmacia) with a modified polylinker
L0805	NCL_CGAP_Lu24				carcinoid	lung	pT7T3D-Pac (Pharmacia) with a modified polylinker

L0806	NCL_CGAP_Lu19	squamous cell carcinoma, poorly differentiated (4	lung			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0807	NCL_CGAP_Ov18	fibrothoma	ovary			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0808	Barstead prostate BPH HP_LRB4_1		prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0809	NCL_CGAP_Pr28		prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0879	BT0254		breast			puc18
L0946	BT0333		breast			puc18
L1057	BT0559		breast			puc18
L1441	CT0249		colon			puc18
L1446	CT0254		colon			puc18
L1499	CT0322		colon			puc18
L1788	HT0229		head_neck			puc18
L1819	HT0268		head_neck			puc18
L1877	HT0340		head_neck			puc18
L1878	HT0342		head_neck			puc18
L2138	ST0186		stomach			puc18
L2174	ST0240		stomach			puc18
L2251	Human fetal lung	Fetal lung				
L2252	Human placenta	placenta				
L2255	GLC	corresponding non cancerous liver tissue				pBluescript sk(-)
L2257	NIH_MGC_65	adenocarcinoma	colon			pCMV-SPORT6
L2258	NIH_MGC_67	retinoblastoma	eye			pCMV-SPORT6
L2259	NIH_MGC_68	large cell carcinoma	lung			pCMV-SPORT6
L2260	NIH_MGC_69	large cell carcinoma, undifferentiated	lung			pCMV-SPORT6

L2261	NIH_MGC_70	epithelioid carcinoma	pancreas			pCMV-SPORT6
L2262	NIH_MGC_72	melanotic melanoma	skin			pCMV-SPORT6
L2263	NIH_MGC_66	adenocarcinoma	ovary			pCMV-SPORT6
L2264	NIH_MGC_71	leiomyosarcoma	uterus			pCMV-SPORT6
L2265	NIH_MGC_39	adenocarcinoma	pancreas			pOTB7
L2270	Lupski_dorsal_root_ganglion	dorsal root ganglia				pCMV-SPORT6 (Life Technologies)
L2289	BT0757		breast			puc18
L2333	CT0417		colon			puc18
L2338	CT0432		colon			puc18
L2346	CT0483		colon			puc18
L2357	UT0021		uterus_tumor			puc18
L2367	UT0039		uterus_tumor			puc18
L2377	NN0054		nervous_normal			puc18
L2380	NN0068		nervous_normal			puc18
L2400	NN0116		nervous_normal			puc18
L2412	NN0136		nervous_normal			puc18
L2413	NN0141		nervous_normal			puc18
L2439	NN1022		nervous_normal			puc18
L2440	NN1023		nervous_normal			puc18
L2491	HT0559		head_neck			puc18
L2495	HT0594		head_neck			puc18
L2497	HT0618		head_neck			puc18
L2504	HT0636		head_neck			puc18
L2518	HT0697		head_neck			puc18
L2519	HT0698		head_neck			puc18
L2522	HT0704		head_neck			puc18
L2539	HT0727		head_neck			puc18
L2540	HT0728		head_neck			puc18
L2543	HT0734		head_neck			puc18
L2550	HT0743		head_neck			puc18
L2570	HT0771		head_neck			puc18

L2598	HT0809			head_neck			puc18
L2634	HT0872			head_neck			puc18
L2637	HT0877			head_neck			puc18
L2640	HT0881			head_neck			puc18
L2647	HT0894			head_neck			puc18
L2650	HT0934			head_neck			puc18
L2651	NIH_MGC_20	melanotic melanoma		skin			pOTB7
L2653	NIH_MGC_58	hypemephroma		kidney			pDNR-LIB (Clontech)
L2654	NIH_MGC_9	adenocarcinoma cell line		ovary			pOTB7
L2655	NIH_MGC_55	from acute myelogenous leukemia		bone marrow			pDNR-LIB (Clontech)
L2657	NIH_MGC_54	from chronic myelogenous leukemia		bone marrow			pDNR-LIB (Clontech)
L2667	NT0013			nervous_tumor			puc18
L2669	NT0022			nervous_tumor			puc18
L2670	NT0023			nervous_tumor			puc18
L2671	NT0024			nervous_tumor			puc18
L2677	NT0039			nervous_tumor			puc18
L2686	NT0058			nervous_tumor			puc18
L2702	NT0098			nervous_tumor			puc18
L2708	NT0104			nervous_tumor			puc18
L2709	NT0105			nervous_tumor			puc18
L2716	NT0117			nervous_tumor			puc18
L2738	GN0049			placenta_normal			puc18
L2767	FT0044			prostate_tumor			puc18
L2791	FT0077			prostate_tumor			puc18
L2799	FT0096			prostate_tumor			puc18
L2804	FT0103			prostate_tumor			puc18
L2817	FT0131			prostate_tumor			puc18
L2831	FT0162			prostate_tumor			puc18
L2842	UM0009			uterus			puc18
L2852	UM0077			uterus			puc18

L2865	AN0004			amniion_normal			puc18
L2877	AN0027			amniion_normal			puc18
L2884	AN0041			amniion_normal			puc18
L2902	BN0036			breast_normal			puc18
L2904	BN0042			breast_normal			puc18
L2905	BN0046			breast_normal			puc18
L2906	BN0047			breast_normal			puc18
L2910	BN0070			breast_normal			puc18
L2915	BN0098			breast_normal			puc18
L2919	BN0115			breast_normal			puc18
L2962	BN0221			breast_normal			puc18
L2991	BN0264			breast_normal			puc18
L2999	BN0273			breast_normal			puc18
L3002	BN0276			breast_normal			puc18
L3019	BN0303			breast_normal			puc18
L3071	EN0026			lung_normal			puc18
L3089	ET0018			lung_tumor			puc18
L3104	ET0041			lung_tumor			puc18
L3111	ET0058			lung_tumor			puc18
L3117	ET0068			lung_tumor			puc18
L3118	ET0070			lung_tumor			puc18
L3119	ET0072			lung_tumor			puc18
L3127	ET0084			lung_tumor			puc18
L3140	MT0031			marrow			puc18
L3153	MT0049			marrow			puc18
L3199	OT0019			ovary			puc18
L3204	OT0034			ovary			puc18
L3207	OT0063			ovary			puc18
L3210	OT0067			ovary			puc18
L3215	OT0083			ovary			puc18
L3216	OT0086			ovary			puc18
L3226	FN0019			prostate_normal			puc18

L3262	FN0073			prostate_normal			puc18
L3281	FN0107			prostate_normal			puc18
L3311	FN0180			prostate_normal			puc18
L3316	FN0188			prostate_normal			puc18
L3327	SN0024			stomach_normal			puc18
L3330	SN0041			stomach_normal			puc18
L3352	TN0027			testis_normal			puc18
L3357	TN0034			testis_normal			puc18
L3372	TN0068			testis_normal			puc18
L3374	TN0070			testis_normal			puc18
L3377	TN0079			testis_normal			puc18
L3387	GKB		hepatocellular carcinoma				pBluescript sk(-)
L3388	GKC		hepatocellular carcinoma				pBluescript sk(-)
L3391	NIH_MGC_53		carcinoma, cell line	bladder			pDNR-LIB (Clontech)
L3402	AN0086			amnion_normal			puc18
L3403	AN0087			amnion_normal			puc18
L3421	BT0634			breast			puc18
L3432	CT0461			colon			puc18
L3435	CT0465			colon			puc18
L3450	CT0508			colon			puc18
L3459	FT0175			prostate_tumor			puc18
L3466	GN0020			placenta_normal			puc18
L3480	GN0057			placenta_normal			puc18
L3484	GN0067			placenta_normal			puc18
L3485	GN0070			placenta_normal			puc18
L3491	GN0076			placenta_normal			puc18
L3496	HT0572			head_neck			puc18
L3499	HT0617			head_neck			puc18
L3503	HT0870			head_neck			puc18
L3504	HT0873			head_neck			puc18
L3506	HT0879			head_neck			puc18
L3511	HT0900			head_neck			puc18

L3516	HT0913			head_neck			puc18
L3518	HT0915			head_neck			puc18
L3521	HT0919			head_neck			puc18
L3530	HT0939			head_neck			puc18
L3561	TN0025			testis_normal			puc18
L3562	TN0030			testis_normal			puc18
L3603	UM0093			uterus			puc18
L3618	UT0050			uterus_tumor			puc18
L3632	UT0074			uterus_tumor			puc18
L3642	ADA	Adrenal gland					pBluescript sk(-)
L3643	ADB	Adrenal gland					pBluescript sk(-)
L3644	ADC	Adrenal gland					pBluescript sk(-)
L3645	Cu	adrenal cortico adenoma for Cushing's syndrome					pBluescript sk(-)
L3646	DCA						pTriplEx2
L3649	DCB						pTriplEx2
L3653	HTB	Hypothalamus					pBluescript sk(-)
L3655	HTC	Hypothalamus					pBluescript sk(-)
L3657	HTF	Hypothalamus					pBluescript sk(-)
L3658	cdA	pheochromocytoma					pTriplEx2
L3659	CB	cord blood					pBluescript
L3661	NPA	pituitary					pBluescript sk(-)
L3665	NIH_MGC_75			kidney			pDNR-LIB (Clontech)
L3667	NIH_MGC_79			placenta			pDNR-LIB (Clontech)
L3673	AN0084			amnion_normal			puc18
L3684	BT0812			breast			puc18
L3705	CT0486			colon			puc18
L3729	GN0079			placenta_normal			puc18
L3744	HT0916			head_neck			puc18
L3750	HT0945			head_neck			puc18
L3783	TN0136			testis_normal			puc18
L3807	UT0077			uterus_tumor			puc18

L3808	UT0078						puc18
L3811	NPC						pBluescript sk(-)
L3812	NPD						pBluescript sk(-)
L3813	TP						pTriplEx2
L3814	BM						pTriplEx2
L3815	MDS						pTriplEx2
L3816	HEMBA1						pME18SFL3
L3817	HEMBA1						pME18SFL3
L3819	NIH_MGC_76						pDNR-LIB (Clontech)
L3824	NT2RM2				liver		pME18SFL3
L3825	NT2RM4					NT2	pME18SFL3
L3826	NT2RP1					NT2	pUC19FL3
L3827	NT2RP2					NT2	pME18SFL3
L3828	NT2RP3					NT2	pME18SFL3
L3829	NT2RP4					NT2	pME18SFL3
L3831	OVARC1						pME18SFL3
L3832	PLACE1			ovary, tumor tissue			pME18SFL3
L3834	PLACE3			placenta			pME18SFL3
L3837	THYRO1			thyroid gland			pME18SFL3
L3841	NIH_MGC_18			large cell carcinoma			pME18SFL3
L3871	NIH_MGC_19			neuroblastoma	lung		pOTB7
L3872	NCL_CGAP_Skn1				brain		pOTB7
					skin, normal, 4 pooled sa		pCMV-SPORT6
L3904	NCL_CGAP_Bm64			glioblastoma with EGFR amplification	brain		pCMV-SPORT6
L3905	NCL_CGAP_Bm67			anaplastic oligodendroglioma with 1p/19q loss	brain		pCMV-SPORT6
L4497	NCL_CGAP_Br22			invasive ductal carcinoma, 3 pooled samples	breast		pCMV-SPORT6

L4501	NCI_CGAP_Sub8					pT7T3D-Pac (Pharmacia) with a modified polylinker
L4537	NCI_CGAP_Thy7	follicular adenoma (benign lesion)	thyroid			pAMP10
L4556	NCI_CGAP_HN13	squamous cell carcinoma	tongue			pCMV-SPORT6
L4558	NCI_CGAP_Pan3		pancreas			pCMV-SPORT6
L4560	NCI_CGAP_Ut7	tumor	uterus			pCMV-SPORT6
L4669	NCI_CGAP_Ov41	serous papillary tumor	ovary			pCMV-SPORT6
L4747	NCI_CGAP_Bm41	oligodendroglioma	brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L5286	NCI_CGAP_Thy10	medullary carcinoma	thyroid			pAMP10
L5564	NCI_CGAP_HN20		normal head/neck tissue			pAMP1
L5565	NCI_CGAP_Bm66	glioblastoma with probably TP53 mutation and witho	brain			pCMV-SPORT6
L5566	NCI_CGAP_Bm70	anaplastic oligodendroglioma	brain			pCMV-SPORT6.cddb
L5568	NCI_CGAP_HN21	nasopharyngeal carcinoma	head/neck			pAMP1
L5569	NCI_CGAP_HN17	normal epithelium	nasopharynx			pAMP10
L5574	NCI_CGAP_HN19	normal epithelium	nasopharynx			pAMP10
L5575	NCI_CGAP_Bm65	glioblastoma without EGFR amplification	brain			pCMV-SPORT6
L5622	NCI_CGAP_Skn3		skin			pCMV-SPORT6
L5623	NCI_CGAP_Skn4	squamous cell carcinoma	skin			pCMV-SPORT6

Description of Table 5

Table 5 provides a key to the OMIM reference identification numbers disclosed in Table 1B.1, column 9. OMIM reference identification numbers (Column 1) were derived from Online Mendelian Inheritance in Man (Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute for Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine, (Bethesda, MD) 2000. World Wide Web URL: <http://www.ncbi.nlm.nih.gov/omim/>). Column 2 provides diseases associated with the cytologic band disclosed in Table 1B.1, column 8, as determined using the Morbid Map database.

Table 5

OMIM Reference	Description
100690	Myasthenic syndrome, slow-channel congenital, 601462
100710	Myasthenic syndrome, slow-channel congenital, 601462
101000	Meningioma, NF2-related, sporadic Schwannoma, sporadic
101000	Neurofibromatosis, type 2
101000	Neurolemmomatosis
101000	Malignant mesothelioma, sporadic
102578	Leukemia, acute promyelocytic, PML/RARA type
102770	Myoadenylate deaminase deficiency
103050	Autism, succinylpurinemic
103050	Adenylosuccinase deficiency
103850	Aldolase A deficiency
104770	Amyloidosis, secondary, susceptibility to
106100	Angioedema, hereditary
106150	Hypertension, essential, susceptibility to
106150	Preeclampsia, susceptibility to
106165	Hypertension, essential, 145500
106180	Myocardial infarction, susceptibility to
107300	Antithrombin III deficiency
107670	Apolipoprotein A-II deficiency
107741	Hyperlipoproteinemia, type III
107777	Diabetes insipidus, nephrogenic, autosomal recessive, 222000
108725	Atherosclerosis, susceptibility to
108985	Atrophia areata
109270	Renal tubular acidosis, distal, 179800
109270	Spherocytosis, hereditary
109270	[Acanthocytosis, one form]
109270	[Elliptocytosis, Malaysian-Melanesian type]
109270	Hemolytic anemia due to band 3 defect
109560	Leukemia/lymphoma, B-cell, 3
109690	Asthma, nocturnal, susceptibility to
109690	Obesity, susceptibility to
109700	Hemodialysis-related amyloidosis
110100	Blepharophimosis, epicanthus inversus, and ptosis, type 1
110700	Vivax malaria, susceptibility to
113100	Brachydactyly, type C

113900	Heart block, progressive familial, type I
114835	Monocyte carboxyesterase deficiency
115665	Cataract, congenital, Volkmann type
116800	Cataract, Marner type
116806	Colorectal cancer
116860	Cavernous angiomatous malformations
117700	[Hypoceruloplasminemia, hereditary]
117700	Hemosiderosis, systemic, due to aceruloplasminemia
118485	Polycystic ovary syndrome with hyperandrogenemia
118800	Choreoathetosis, familial paroxysmal
120070	Alport syndrome, autosomal recessive, 203780
120131	Alport syndrome, autosomal recessive, 203780
120131	Hematuria, familial benign
120140	Osteoarthritis, precocious
120140	SED congenita
120140	SMED Strudwick type
120140	Stickler syndrome, type I
120140	Wagner syndrome, type II
120140	Achondrogenesis-hypochondrogenesis, type II
120140	Kniest dysplasia
120150	Osteogenesis imperfecta, 4 clinical forms, 166200, 166210, 259420, 166220
120150	Osteoporosis, idiopathic, 166710
120150	Ehlers-Danlos syndrome, type VIIA1, 130060
120215	Ehlers-Danlos syndrome, type I, 130000
120215	Ehlers-Danlos syndrome, type II, 130010
120260	Epiphyseal dysplasia, multiple, type 2, 600204
120435	Muir-Torre syndrome, 158320
120435	Colorectal cancer, hereditary, nonpolyposis, type I Ovarian cancer
120550	Clq deficiency, type A
120570	Clq deficiency, type B
120575	Clq deficiency, type C
120700	C3 deficiency
120950	C8 deficiency, type I
120960	C8 deficiency, type II
121050	Contractural arachnodactyly, congenital
121360	Myeloid leukemia, acute, M4Eo subtype
121800	Corneal dystrophy, crystalline, Schnyder
122720	Nicotine addiction, protection from
122720	Coumarin resistance, 122700
123000	Craniometaphyseal dysplasia
123270	[Creatine kinase, brain type, ectopic expression of]
123620	Cataract, cerulean, type 2, 601547
123660	Cataract, Coppock-like
123940	White sponge nevus, 193900
124030	Parkinsonism, susceptibility to
124030	Debrisoquine sensitivity
124200	Darier disease (keratosis follicularis)
125370	Dentatorubro-pallidoluysian atrophy
125660	Myopathy, desminopathic
125660	Cardiomyopathy
126090	Hyperphenylalaninemia due to pterin-4a-carbinolamine dehydratase

	deficiency, 264070
126337	Myxoid liposarcoma
126340	Xeroderma pigmentosum, group D, 278730
126391	DNA ligase I deficiency
126600	Drusen, radial, autosomal dominant
129010	Neuropathy, congenital hypomyelinating, 1
129900	EEC syndrome-1
130410	Glutaricaciduria, type IIB
130500	Elliptocytosis-1
131210	Atherosclerosis, susceptibility to
131244	Hirschsprung disease-2, 600155
131400	Eosinophilia, familial
132700	Cylindromatosis
133171	[Erythrocytosis, familial], 133100
133200	Erythrokeratoderma variabilis
133530	Xeroderma pigmentosum, group G, 278780
133701	Exostoses, multiple, type 2
133780	Vitreoretinopathy, exudative, familial
134790	Hyperferritinemia-cataract syndrome, 600886
135300	Fibromatosis, gingival
135940	Ichthyosis vulgaris, 146700
136132	[Fish-odor syndrome], 602079
136350	Pfeiffer syndrome, 101600
136435	Ovarian dysgenesis, hypergonadotropic, with normal karyotype, 233300
136550	Macular dystrophy, North Carolina type
136836	Fucosyltransferase-6 deficiency
138030	[Hyperproglucagonemia]
138040	Cortisol resistance
138140	Glucose transport defect, blood-brain barrier
138160	Diabetes mellitus, noninsulin-dependent
138160	Fanconi-Bickel syndrome, 227810
138300	Hemolytic anemia due to glutathione reductase deficiency
138570	Non-insulin dependent diabetes mellitus, susceptibility to
138700	[Apolipoprotein H deficiency]
138981	Pulmonary alveolar proteinosis, 265120
139250	Isolated growth hormone deficiency, Illig type with absent GH and Kowarski type with bioinactive GH
139350	Epidermolytic hyperkeratosis, 113800
139350	Keratoderma, palmoplantar, nonepidermolytic
140100	[Anhaptoglobinemia]
140100	[Hypohaptoglobinemia]
141750	Alpha-thalassemia/mental retardation syndrome, type 1
141800	Methemoglobinemias, alpha-
141800	Thalassemias, alpha-
141800	Erythremias, alpha-
141800	Heinz body anemias, alpha-
141850	Thalassemia, alpha-
141850	Erythrocytosis
141850	Heinz body anemia
141850	Hemoglobin H disease
141850	Hypochromic microcytic anemia

142335	Hereditary persistence of fetal hemoglobin, heterocellular, Indian type
142600	Hemolytic anemia due to hexokinase deficiency
142989	Synpolydactyly, type II, 186000
143890	Hypercholesterolemia, familial
145001	Hyperparathyroidism-jaw tumor syndrome
145260	Pseudohypoaldosteronism, type II
145505	Hypertension, essential
145981	Hypocalciuric hypercalcemia, type II
146200	Hypoparathyroidism, familial
146760	[IgG receptor I, phagocytic, familial deficiency of]
146790	Lupus nephritis, susceptibility to
147141	Leukemia, acute lymphoblastic
147440	Growth retardation with deafness and mental retardation
147670	Rabson-Mendenhall syndrome
147670	Diabetes mellitus, insulin-resistant, with acanthosis nigricans
147670	Leprechaunism
147781	Atopy, susceptibility to
148040	Epidermolysis bullosa simplex, Koebner, Dowling-Meara, and Weber-Cockayne types, 131900, 131760, 131800
148041	Pachyonychia congenita, Jadassohn-Lewandowsky type, 167200
148043	Meesmann corneal dystrophy, 122100
148065	White sponge nevus, 193900
148070	Liver disease, susceptibility to, from hepatotoxins or viruses
148080	Epidermolytic hyperkeratosis, 113800
148370	Keratolytic winter erythema
148900	Klippel-Feil syndrome with laryngeal malformation
150200	[Placental lactogen deficiency]
150210	Lactoferrin-deficient neutrophils, 245480
150292	Epidermolysis bullosa, Herlitz junctional type, 226700
151440	Leukemia, T-cell acute lymphoblastoid
151670	Hepatic lipase deficiency
152427	Long QT syndrome-2
152445	Vohwinkel syndrome, 124500
152445	Erythrokeratoderma, progressive symmetric, 602036
152760	Hypogonadotropic hypogonadism due to GNRH deficiency, 227200
152780	Hypogonadism, hypergonadotropic
152780	Male pseudohermaphroditism due to defective LH
152790	Precocious puberty, male, 176410
152790	Leydig cell hypoplasia
153454	Ehlers-Danlos syndrome, type VI, 225400
153455	Cutis laxa, recessive, type I, 219100
154275	Malignant hyperthermia susceptibility 2
154276	Malignant hyperthermia susceptibility 3
154545	Chronic infections, due to opsonin defect
154550	Carbohydrate-deficient glycoprotein syndrome, type Ib, 602579
155555	[Red hair/fair skin]
155555	UV-induced skin damage, vulnerability to
156232	Mesomelic dysplasia, Kantaputra type
156850	Cataract, congenital, with microphthalmia
157147	Abetalipoproteinemia, 200100

157170	Holoprosencephaly-2
157640	PEO with mitochondrial DNA deletions, type 1
158590	Spinal muscular atrophy-4
159000	Muscular dystrophy, limb-girdle, type 1A
159001	Muscular dystrophy, limb-girdle, type 1B
160760	Cardiomyopathy, familial hypertrophic, 1, 192600
160760	Central core disease, one form
160781	Cardiomyopathy, hypertrophic, mid-left ventricular chamber type
160900	Myotonic dystrophy
162150	Obesity with impaired prohormone processing, 600955
162200	Neurofibromatosis, type 1
162200	Watson syndrome, 193520
162400	Neuropathy, hereditary sensory and autonomic, type 1
163729	Hypertension, pregnancy-induced
163950	Noonan syndrome-1
163950	Cardiofaciocutaneous syndrome, 115150
164731	Ovarian carcinoma, 167000
164770	Myeloid malignancy, predisposition to
164953	Liposarcoma
167410	Rhabdomyosarcoma, alveolar, 268220
168360	Paraneoplastic sensory neuropathy
168450	Hypoparathyroidism, autosomal dominant
168450	Hypoparathyroidism, autosomal recessive
168468	Metaphyseal chondrodysplasia, Murk Jansen type, 156400
168500	Parietal foramina
169600	Hailey-Hailey disease
170500	Myotonia congenita, atypical acetazolamide-responsive
170500	Paramyotonia congenita, 168300
170500	Hyperkalemic periodic paralysis
171190	Hypertension, essential, 145500
171650	Lysosomal acid phosphatase deficiency
171760	Hypophosphatasia, adult, 146300
171760	Hypophosphatasia, infantile, 241500
172400	Hemolytic anemia due to glucosephosphate isomerase deficiency
172400	Hydrops fetalis, one form
172430	Enolase deficiency
172471	Glycogenosis, hepatic, autosomal
172490	Phosphorylase kinase deficiency of liver and muscle, 261750
173470	Glanzmann thrombasthenia, type B
173610	Platelet alpha/delta storage pool deficiency
173850	Polio, susceptibility to
173870	Xeroderma pigmentosum
173870	Fanconi anemia
173910	Polycystic kidney disease, adult, type II
174000	Medullary cystic kidney disease, AD
174900	Polyposis, juvenile intestinal
176100	Porphyria cutanea tarda
176100	Porphyria, hepatoerythropoietic
176450	Sacral agenesis-1
176830	Obesity, adrenal insufficiency, and red hair
176830	ACTH deficiency
176930	Dysprothrombinemia

176930	Hypoprothrombinemia
176960	Pituitary tumor, invasive
177400	Apnea, postanesthetic
178300	Ptosis, hereditary congenital, 1
178600	Pulmonary hypertension, familial primary
178640	Pulmonary alveolar proteinosis, congenital, 265120
179095	Male infertility
179755	Renal cell carcinoma, papillary, 1
180069	Retinal dystrophy, autosomal recessive, childhood-onset
180069	Retinitis pigmentosa-20
180069	Leber congenital amaurosis-2, 204100
180071	Retinitis pigmentosa, autosomal recessive
180100	Retinitis pigmentosa-1
180105	Retinitis pigmentosa-10
180380	Night blindness, congenital stationary, rhodopsin-related
180380	Retinitis pigmentosa, autosomal recessive
180380	Retinitis pigmentosa-4, autosomal dominant
180901	Malignant hyperthermia susceptibility 1, 145600
180901	Central core disease, 117000
181405	Scapuloperoneal spinal muscular atrophy, New England type
181430	Scapuloperoneal syndrome, myopathic type
181460	Schistosoma mansoni, susceptibility/resistance to
182138	Anxiety-related personality traits
182280	Small-cell cancer of lung
182290	Smith-Magenis syndrome
182380	Glucose/galactose malabsorption
182381	Renal glucosuria, 253100
182600	Spastic paraplegia-3A
182601	Spastic paraplegia-4
182860	Pyropoikilocytosis
182860	Spherocytosis, recessive
182860	Elliptocytosis-2
182900	Spherocytosis-2
185800	Symphalangism, proximal
186580	Arthrocuteaneuveal granulomatosis
186880	Leukemia/lymphoma, T-cell
186921	Leukemia, T-cell acute lymphoblastic
187040	Leukemia-1, T-cell acute lymphoblastic
188070	Bleeding disorder due to defective thromboxane A2 receptor
188450	Goiter, adolescent multinodular
188450	Goiter, nonendemic, simple
188450	Hypothyroidism, hereditary congenital
188826	Sorsby fundus dystrophy, 136900
189800	Preeclampsia/eclampsia
190040	Meningioma, SIS-related
190040	Dermatofibrosarcoma protuberans
190040	Giant-cell fibroblastoma
190195	Ichthyosiform erythroderma, congenital, 242100
190195	Ichthyosis, lamellar, autosomal recessive, 242300
190198	Leukemia, T-cell acute lymphoblastic
190300	Tremor, familial essential, 1
190605	Triphalangeal thumb-polysyndactyly syndrome

191044	Cardiomyopathy, familial hypertrophic
191092	Tuberous sclerosis-2
191315	Insensitivity to pain, congenital, with anhidrosis, 256800
192090	Ovarian carcinoma
192090	Breast cancer, lobular
192090	Endometrial carcinoma
192090	Gastric cancer, familial, 137215
192340	Diabetes insipidus, neurohypophyseal, 125700
192974	Neonatal alloimmune thrombocytopenia
192974	Glycoprotein Ia deficiency
193300	Renal cell carcinoma
193300	von Hippel-Lindau syndrome
193500	Rhabdomyosarcoma, alveolar, 268220
193500	Waardenburg syndrome, type I
193500	Waardenburg syndrome, type III, 148820
193500	Craniofacial-deafness-hand syndrome, 122880
201450	Acyl-CoA dehydrogenase, medium chain, deficiency of
201460	Acyl-CoA dehydrogenase, long chain, deficiency of
201475	VLCAD deficiency
201810	3-beta-hydroxysteroid dehydrogenase, type II, deficiency
203300	Hermansky-Pudlak syndrome
203500	Alkaptonuria
205100	Amyotrophic lateral sclerosis, juvenile
205900	Anemia, Diamond-Blackfan
207750	Hyperlipoproteinemia, type Ib
208250	Jacobs syndrome
208400	Aspartylglucosaminuria
212138	Carnitine-acylcarnitine translocase deficiency
216550	Cohen syndrome
216900	Achromatopsia
217300	Cornea plana congenita, recessive
217800	Macular corneal dystrophy
218030	Apparent mineralocorticoid excess, hypertension due to
221770	Polycystic lipomembranous osteodysplasia with sclerosing leukencephalopathy
221820	Gliososis, familial progressive subcortical
222700	Lysinuric protein intolerance
222745	DECR deficiency
222800	Hemolytic anemia due to bisphosphoglycerate mutase deficiency
222900	Sucrose intolerance
225500	Ellis-van Creveld syndrome
227645	Fanconi anemia, type C
227646	Fanconi anemia, type D
227650	Fanconi anemia, type A
229700	Fructose-bisphosphatase deficiency
229800	[Fructosuria]
230000	Fucosidosis
230400	Galactosemia
230800	Gaucher disease
230800	Gaucher disease with cardiovascular calcification
231550	Achalasia-addisonianism-alacrimia syndrome
231670	Glutaricaciduria, type I

231675	Glutaricaciduria, type IIC
231680	Glutaricaciduria, type IIA
232300	Glycogen storage disease II
232700	Glycogen storage disease VI
232800	Glycogen storage disease VII
233700	Chronic granulomatous disease due to deficiency of NCF-1
234200	Neurodegeneration with brain iron accumulation
236250	Homocystinuria due to MTHFR deficiency
236730	Urofacial syndrome
237300	Carbamoylphosphate synthetase I deficiency
239100	Van Buchem disease
240400	Scurvy
245200	Krabbe disease
245900	Norum disease
245900	Fish-eye disease
246450	HMG-CoA lyase deficiency
248510	Mannosidosis, beta-
248600	Maple syrup urine disease, type Ia
248610	Maple syrup urine disease, type II
249000	Meckel syndrome
250250	Cartilage-hair hypoplasia
250790	Methemoglobinemia due to cytochrome b5 deficiency
250850	Hypermethioninemia, persistent, autosomal dominant, due to methionine adenosyltransferase I/III deficiency
251170	Mevalonicaciduria
251600	Microphthalmia, autosomal recessive
252500	Mucopolipidosis II
252500	Mucopolipidosis III
252900	Sanfilippo syndrome, type A
253000	Mucopolysaccharidosis IVA
253250	Mulibrey nanism
255800	Schwartz-Jampel syndrome
256030	Nemaline myopathy-2
256540	Galactosialidosis
256700	Neuroblastoma
256731	Ceroid-lipofuscinosis, neuronal-5, variant late infantile
257200	Niemann-Pick disease, type A
257200	Niemann-Pick disease, type B
258501	3-methylglutaconicaciduria, type III
258900	Oroticaciduria
259900	Hyperoxaluria, primary, type 1
262000	Bjornstad syndrome
266200	Anemia, hemolytic, due to PK deficiency
270100	Situs inversus viscerum
270200	Sjogren-Larsson syndrome
272750	GM2-gangliosidosis, AB variant
272800	Tay-Sachs disease
272800	[Hex A pseudodeficiency]
272800	GM2-gangliosidosis, juvenile, adult
273800	Thrombocytopenia, neonatal alloimmune
273800	Glanzmann thrombasthenia, type A
276600	Tyrosinemia, type II

276700	Tyrosinemia, type I
276710	Tyrosinemia, type III
276900	Usher syndrome, type 1A
276901	Usher syndrome, type 2
276902	Usher syndrome, type 3
277700	Werner syndrome
278700	Xeroderma pigmentosum, group A
278760	Xeroderma pigmentosum, group F
300000	Opitz G syndrome, type I
300008	Nephrolithiasis, type I, 310468
300008	Proteinuria, low molecular weight, with hypercalciuric nephrocalcinosis
300008	Dent disease, 300009
300008	Hypophosphatemia, type III
300011	Menkes disease, 309400
300011	Occipital horn syndrome, 304150
300011	Cutis laxa, neonatal
300031	Mental retardation, X-linked, FRAXF type
300044	Wernicke-Korsakoff syndrome, susceptibility to
300046	Mental retardation, X-linked 23, nonspecific
300047	Mental retardation, X-linked 20
300048	Intestinal pseudoobstruction, neuronal, X-linked
300049	Nodular heterotopia, bilateral periventricular
300049	BPNH/MR syndrome
300055	Mental retardation with psychosis, pyramidal signs, and macroorchidism
300066	Deafness, X-linked 6, sensorineural
300071	Night blindness, congenital stationary, type 2
300075	Coffin-Lowry syndrome, 303600
300077	Mental retardation, X-linked 29
300100	Adrenoleukodystrophy
300100	Adrenomyeloneuropathy
300104	Mental retardation, X-linked nonspecific, 309541
300110	Night blindness, congenital stationary, X-linked incomplete, 300071
300123	Mental retardation with isolated growth hormone deficiency
300126	Dyskeratosis congenita-1, 305000
300127	Mental retardation, X-linked, 60
300310	Agammaglobulinemia, type 2, X-linked
300600	Ocular albinism, Forsius-Eriksson type
301000	Thrombocytopenia, X-linked, 313900
301000	Wiskott-Aldrich syndrome
301200	Amelogenesis imperfecta
301201	Amelogenesis imperfecta-3, hypoplastic type
301220	Partington syndrome II
301590	Anophthalmos-I
301830	Arthrogryposis, X-linked (spinal muscular atrophy, infantile, X-linked)
301835	Arts syndrome
301845	Bazex syndrome
302060	Noncompaction of left ventricular myocardium, isolated
302060	Barth syndrome

302060	Cardiomyopathy, X-linked dilated, 300069
302060	Endocardial fibroelastosis-2
302350	Nance-Horan syndrome
302801	Charcot-Marie-Tooth neuropathy, X-linked-2, recessive
302960	Chondrodysplasia punctata, X-linked dominant
303700	Colorblindness, blue monochromatic
303800	Colorblindness, deutan
303900	Colorblindness, protan
304040	Charcot-Marie-Tooth neuropathy, X-linked-1, dominant, 302800
304050	Aicardi syndrome
304110	Craniofrontonasal dysplasia
304800	Diabetes insipidus, nephrogenic
305100	Anhidrotic ectodermal dysplasia
305435	Heterocellular hereditary persistence of fetal hemoglobin, Swiss type
305450	FG syndrome
305900	Favism
305900	G6PD deficiency
305900	Hemolytic anemia due to G6PD deficiency
306000	Glycogenosis, X-linked hepatic, type I
306000	Glycogenosis, X-linked hepatic, type II
306100	Gonadal dysgenesis, XY female type
306700	Hemophilia A
306995	[Homosexuality, male]
307150	Hypertrichosis, congenital generalized
307800	Hypophosphatemia, hereditary
308310	Incontinentia pigmenti, familial
308800	Keratosis follicularis spinulosa decalvans
308840	Spastic paraplegia, 312900
308840	Hydrocephalus due to aqueductal stenosis, 307000
308840	MASA syndrome, 303350
309200	Manic-depressive illness, X-linked
309470	Mental retardation, X-linked, syndromic-3, with spastic diplegia
309500	Renpenning syndrome-1
309510	Mental retardation, X-linked, syndromic-1, with dystonic movements, ataxia, and seizures
309530	Mental retardation, X-linked 1, non-dysmorphic
309548	Mental retardation, X-linked, FRAXE type
309585	Mental retardation, X-linked, syndromic-6, with gynecomastia and obesity
309605	Mental retardation, X-linked, syndromic-4, with congenital contractures and low fingertip arches
309610	Mental retardation, X-linked, syndromic-2, with dysmorphism and cerebral atrophy
309620	Mental retardation-skeletal dysplasia
309850	Brunner syndrome
309900	Mucopolysaccharidosis II
310300	Emery-Dreifuss muscular dystrophy
310400	Myotubular myopathy, X-linked
310460	Myopia-1
310460	Bornholm eye disease
310490	Cowchock syndrome

311050	Optic atrophy, X-linked
311200	Oral-facial-digital syndrome 1
311300	Otopalatodigital syndrome, type I
311510	Waisman parkinsonism-mental retardation syndrome
311850	Phosphoribosyl pyrophosphate synthetase-related gout
312040	N syndrome, 310465
312060	Properdin deficiency, X-linked
312170	Pyruvate dehydrogenase deficiency
312700	Retinoschisis
312760	Turner syndrome
313400	Spondyloepiphyseal dysplasia tarda
313700	Perineal hypospadias
313700	Prostate cancer
313700	Spinal and bulbar muscular atrophy of Kennedy, 313200
313700	Breast cancer, male, with Reifenstein syndrome
313700	Androgen insensitivity, several forms
314250	Dystonia-3, torsion, with parkinsonism, Filipino type
314300	Goeminne TKCR syndrome
314400	Cardiac valvular dysplasia-1
314580	Wieacker-Wolff syndrome
600040	Colorectal cancer
600079	Colon cancer
600101	Deafness, autosomal dominant 2
600119	Muscular dystrophy, Duchenne-like, type 2
600119	Adhalinopathy, primary
600138	Retinitis pigmentosa-11
600140	Rubenstein-Taybi syndrome, 180849
600163	Long QT syndrome-3
600173	SCID, autosomal recessive, T-negative/B-positive type
600175	Spinal muscular atrophy, congenital nonprogressive, of lower limbs
600194	Ichthyosis bullosa of Siemens, 146800
600223	Spinocerebellar ataxia-4
600231	Palmoplantar keratoderma, Bothnia type
600234	HMG-CoA synthase-2 deficiency
600243	Temperature-sensitive apoptosis
600258	Colorectal cancer, hereditary nonpolyposis, type 3
600266	Resistance/susceptibility to TB, etc.
600273	Polycystic kidney disease, infantile severe, with tuberous sclerosis
600276	Cerebral arteriopathy with subcortical infarcts and leukoencephalopathy, 125310
600281	Non-insulin-dependent diabetes mellitus, 125853
600281	MODY, type 1, 125850
600309	Atrioventricular canal defect-1
600310	Pseudoachondroplasia, 177170
600310	Epiphyseal dysplasia, multiple 1, 132400
600320	Insulin-dependent diabetes mellitus-5
600332	Rippling muscle disease-1
600359	Bartter syndrome, type 2
600374	Bardet-Biedl syndrome 4
600510	Pigment dispersion syndrome
600512	Epilepsy, partial
600525	Trichodontoosseous syndrome, 190320

600536	Myopathy, congenital
600593	Craniosynostosis, Adelaide type
600617	Lipoid adrenal hyperplasia, 201710
600623	Prostate cancer, 176807
600631	Enuresis, nocturnal, 1
600650	Myopathy due to CPT II deficiency, 255110
600650	CPT deficiency, hepatic, type II, 600649
600652	Deafness, autosomal dominant 4
600698	Salivary adenoma
600698	Uterine leiomyoma
600698	Lipoma
600698	Lipomatosis, mutiple, 151900
600722	Ceroid lipofuscinosis, neuronal, variant juvenile type, with granular osmiophilic deposits
600722	Ceroid lipofuscinosis, neuronal-1, infantile, 256730
600725	Holoprosencephaly-3, 142945
600757	Orofacial cleft-3
600759	Alzheimer disease-4
600792	Deafness, autosomal recessive 5
600807	Bronchial asthma
600808	Enuresis, nocturnal, 2
600811	Xeroderma pigmentosum, group E, DDB-negative subtype, 278740
600850	Schizophrenia disorder-4
600852	Retinitis pigmentosa-17
600881	Cataract, congenital, zonular, with sutural opacities
600882	Charcot-Marie-Tooth neuropathy-2B
600897	Cataract, zonular pulverulent-1, 116200
600918	Cystinuria, type III
600956	Persistent Mullerian duct syndrome, type II, 261550
600957	Persistent Mullerian duct syndrome, type I, 261550
600958	Cardiomyopathy, familial hypertrophic, 4, 115197
600968	Gitelman syndrome, 263800
600975	Glaucoma 3, primary infantile, B
600995	Nephrotic syndrome, idiopathic, steroid-resistant
600996	Arrhythmogenic right ventricular dysplasia-2
601097	Neuropathy, recurrent, with pressure palsies, 162500
601097	Charcot-Marie-Tooth neuropathy-1A, 118220
601097	Dejerine-Sottas disease, PMP22 related, 145900
601105	Pycnodysostosis, 265800
601199	Neonatal hyperparathyroidism, 239200
601199	Hypocalcemia, autosomal dominant, 601198
601199	Hypocalciuric hypercalcemia, type I, 145980
601238	Cerebellar ataxia, Cayman type
601277	Ichthyosis, lamellar, type 2
601284	Hereditary hemorrhagic telangiectasia-2, 600376
601295	Bile acid malabsorption, primary
601309	Basal cell carcinoma, sporadic
601309	Basal cell nevus syndrome, 109400
601313	Polycystic kidney disease, adult type I, 173900
601369	Deafness, autosomal dominant 9
601386	Deafness, autosomal recessive 12
601402	Leukemia, myeloid, acute

601412	Deafness, autosomal dominant 7
601414	Retinitis pigmentosa-18
601458	Inflammatory bowel disease-2
601493	Cardiomyopathy, dilated 1C
601517	Spinocerebellar ataxia-2, 183090
601518	Prostate cancer, hereditary, 1, 176807
601596	Charcot-Marie-Tooth neuropathy, demyelinating
601604	Mycobacterial and salmonella infections, susceptibility to
601650	Paraganglioma, familial nonchromaffin, 2
601652	Glaucoma 1A, primary open angle, juvenile-onset, 137750
601669	Hirschsprung disease, one form
601676	Acute insulin response
601682	Glaucoma 1C, primary open angle
601691	Retinitis pigmentosa-19, 601718
601691	Stargardt disease-1, 248200
601691	Cone-rod dystrophy 3
601691	Fundus flavimaculatus with macular dystrophy, 248200
601692	Reis-Bucklers corneal dystrophy
601692	Corneal dystrophy, Avellino type
601692	Corneal dystrophy, Groenouw type I, 121900
601692	Corneal dystrophy, lattice type I, 122200
601718	Retinitis pigmentosa-19
601744	Systemic lupus erythematosus, susceptibility to, 1
601769	Osteoporosis, involutional
601769	Rickets, vitamin D-resistant, 277440
601771	Glaucoma 3A, primary infantile, 231300
601780	Ceroid-lipofuscinosis, neuronal-6, variant late infantile
601785	Carbohydrate-deficient glycoprotein syndrome, type I, 212065
601843	Hypothyroidism, congenital, 274400
601844	Pseudohypoaldosteronism type II
601846	Muscular dystrophy with rimmed vacuoles
601863	Bare lymphocyte syndrome, complementation group C
601928	Monilethrix, 158000
601954	Muscular dystrophy, limb-girdle, type 2G
601975	Ectodermal dysplasia/skin fragility syndrome
602025	Obesity/hyperinsulinism, susceptibility to
602078	Fibrosis of extraocular muscles, congenital, 2
602085	Postaxial polydactyly, type A2
602086	Arrhythmogenic right ventricular dysplasia-3
602088	Nephronophthisis, infantile
602089	Hemangioma, capillary, hereditary
602092	Deafness, autosomal recessive 18
602094	Lipodystrophy, familial partial
602116	Glioma
602121	Deafness, autosomal dominant nonsyndromic sensorineural, 1, 124900
602134	Tremor, familial essential, 2
602136	Refsum disease, infantile, 266510
602136	Zellweger syndrome-1, 214100
602136	Adrenoleukodystrophy, neonatal, 202370
602153	Monilethrix, 158000
602216	Peutz-Jeghers syndrome, 175200

602225	Cone-rod retinal dystrophy-2, 120970
602225	Leber congenital amaurosis, type III
602279	Oculopharyngeal muscular dystrophy, 164300
602279	Oculopharyngeal muscular dystrophy, autosomal recessive, 257950
602363	Ellis-van Creveld-like syndrome
602403	Alzheimer disease, susceptibility to
602447	Coronary artery disease, susceptibility to
602460	Deafness, autosomal dominant 15, 602459
602477	Febrile convulsions, familial, 2
602491	Hyperlipidemia, familial combined, 1
602522	Bartter syndrome, infantile, with sensorineural deafness
602568	Homocystinuria-megaloblastic anemia, cbl E type, 236270
602574	Deafness, autosomal dominant 12, 601842
602574	Deafness, autosomal dominant 8, 601543
602629	Dystonia-6, torsion
602666	Deafness, autosomal recessive 3, 600316
602716	Nephrosis-1, congenital, Finnish type, 256300
602772	Retinitis pigmentosa-24
602782	Faisalabad histiocytosis
602783	Spastic paraplegia-7

Mature Polypeptides

The present invention also encompasses mature forms of a polypeptide having the amino acid sequence of SEQ ID NO:Y and/or the amino acid sequence encoded by the cDNA in a deposited clone. Polynucleotides encoding the mature forms (such as, for example, the polynucleotide sequence in SEQ ID NO:X and/or the polynucleotide sequence contained in the cDNA of a deposited clone) are also encompassed by the invention. Moreover, fragments or variants of these polypeptides (such as, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to these polypeptides, or polypeptides encoded by a polynucleotide that hybridizes under stringent conditions to the complementary strand of the polynucleotide encoding these polypeptides) are also encompassed by the invention. In preferred embodiments, these fragments or variants retain one or more functional activities of the full-length or mature form of the polypeptide (e.g., biological activity (such as, for example, activity useful in detecting, preventing, diagnosing, prognosticating, treating, and/or ameliorating cancer and other hyperproliferative disorders), antigenicity (ability to bind, or compete with a polypeptide of the invention for binding, to an anti-polypeptide of the invention antibody), immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide of the invention). Antibodies that bind the polypeptides of the invention, and polynucleotides encoding these polypeptides are also encompassed by the invention.

According to the signal hypothesis, proteins secreted by mammalian cells have a signal or secretory leader sequence which is cleaved from the mature protein once export of the growing protein chain across the rough endoplasmic reticulum has been initiated. Most mammalian cells and even insect cells cleave secreted proteins with the same specificity. However, in some cases, cleavage of a secreted protein is not entirely uniform, which results in two or more mature species of the protein. Further, it has long been known that cleavage specificity of a secreted protein is ultimately determined by the primary structure of the complete protein, that is, it is inherent in the amino acid sequence of the polypeptide.

Methods for predicting whether a protein has a signal sequence, as well as the cleavage point for that sequence, are available. For instance, the method of McGeoch, *Virus Res.* 3:271-286 (1985), uses the information from a short N-terminal charged region and a subsequent uncharged region of the complete (uncleaved) protein. The method of von Heinje, *Nucleic Acids Res.* 14:4683-4690 (1986) uses the information from the residues surrounding the cleavage site, typically residues -13 to +2, where +1 indicates the amino terminus of the secreted protein. The accuracy of predicting the cleavage points of known mammalian secretory proteins for each of these methods is in the range of 75-80%. (von Heinje, *supra.*) However, the two methods do not always produce the same predicted cleavage point(s) for a given protein.

In the present case, the deduced amino acid sequence of the secreted polypeptide was analyzed by a computer program called SignalP (Henrik Nielsen et al., *Protein Engineering* 10:1-6 (1997)), which predicts the cellular location of a protein based on the amino acid sequence. As part of this computational prediction of localization, the methods of McGeoch and von Heinje are incorporated. The analysis of the amino acid sequences of the secreted proteins described herein by this program provided the results shown in Table 1A.

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the predicted mature form of the polypeptide as delineated in columns 14 and 15 of Table 1A. Moreover, fragments or variants of these polypeptides (such as, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to these polypeptides, or polypeptides encoded by a polynucleotide that hybridizes under stringent conditions to the complementary strand of the polynucleotide encoding these polypeptides) are also encompassed by the invention. In preferred embodiments, these fragments or variants retain one or more functional activities of the full-length or mature form of the polypeptide (e.g., biological activity (such as, for example, activity useful in detecting, preventing, diagnosing, prognosticating, treating, and/or ameliorating cancer and other hyperproliferative disorders), antigenicity (ability to bind, or compete with a polypeptide of the invention for binding, to an anti-polypeptide of the invention antibody), immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide of the invention).

Antibodies that bind the polypeptides of the invention, and polynucleotides encoding these polypeptides are also encompassed by the invention.

Polynucleotides encoding proteins comprising, or consisting of, the predicted mature form of polypeptides of the invention (e.g., polynucleotides having the sequence of SEQ ID NO: X (Table 1A, column 4), the sequence delineated in columns 7 and 8 of Table 1A, and a sequence encoding the mature polypeptide delineated in columns 14 and 15 of Table 1A (e.g., the sequence of SEQ ID NO: X encoding the mature polypeptide delineated in columns 14 and 15 of Table 1)) are also encompassed by the invention, as are fragments or variants of these polynucleotides (such as, fragments as described herein, polynucleotides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to these polynucleotides, and nucleic acids which hybridizes under stringent conditions to the complementary strand of the polynucleotide).

As one of ordinary skill would appreciate, however, cleavage sites sometimes vary from organism to organism and cannot be predicted with absolute certainty. Accordingly, the present invention provides secreted polypeptides having a sequence shown in SEQ ID NO: Y which have an N-terminus beginning within 15 residues of the predicted cleavage point (i.e., having 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 more or less contiguous residues of SEQ ID NO: Y at the N-terminus when compared to the predicted mature form of the polypeptide (e.g., the mature polypeptide delineated in columns 14 and 15 of Table 1). Similarly, it is also recognized that in some cases, cleavage of the signal sequence from a secreted protein is not entirely uniform, resulting in more than one secreted species. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Moreover, the signal sequence identified by the above analysis may not necessarily predict the naturally occurring signal sequence. For example, the naturally occurring signal sequence may be further upstream from the predicted signal sequence. However, it is likely that the predicted signal sequence will be capable of directing the secreted protein to the ER. Nonetheless, the present invention provides the mature protein produced by expression of the polynucleotide sequence of SEQ ID NO: X and/or the polynucleotide sequence contained in the cDNA of a deposited clone, in a mammalian cell (e.g., COS cells, as described below). These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Polynucleotide and Polypeptide Variants

The present invention is also directed to variants of the polynucleotide sequence disclosed in SEQ ID NO: X or the complementary strand thereto, nucleotide sequences encoding the polypeptide of SEQ ID NO: Y, the nucleotide sequence of SEQ ID NO: X that encodes the polypeptide sequence as defined in columns 13 and 14 of Table 1A, nucleotide sequences encoding the polypeptide sequence as defined in columns 13 and 14 of Table 1A, the nucleotide

sequence of SEQ ID NO:X encoding the polypeptide sequence as defined in Table 1B, the nucleotide sequence as defined in columns 8 and 9 of Table 2, nucleotide sequences encoding the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2, the nucleotide sequence as defined in column 6 of Table 1C, nucleotide sequences encoding the polypeptide encoded by the nucleotide sequence as defined in column 6 of Table 1C, the cDNA sequence contained in ATCC Deposit No:Z, nucleotide sequences encoding the polypeptide encoded by the cDNA sequence contained in ATCC Deposit No:Z, and/or nucleotide sequences encoding a mature (secreted) polypeptide encoded by the cDNA sequence contained in ATCC Deposit No:Z.

10 The present invention also encompasses variants of the polypeptide sequence disclosed in SEQ ID NO:Y, the polypeptide as defined in columns 13 and 14 of Table 1A, the polypeptide sequence as defined in columns 6 and 7 of Table 1B.1, a polypeptide sequence encoded by the polynucleotide sequence in SEQ ID NO:X, a polypeptide sequence encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2, a polypeptide sequence encoded by the
15 nucleotide sequence as defined in column 6 of Table 1C, a polypeptide sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X, the polypeptide sequence encoded by the cDNA sequence contained in ATCC Deposit No:Z and/or a mature (secreted) polypeptide encoded by the cDNA sequence contained in ATCC Deposit No:Z.

"Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or
20 polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

Thus, one aspect of the invention provides an isolated nucleic acid molecule comprising, or alternatively consisting of, a polynucleotide having a nucleotide sequence selected from the
25 group consisting of: (a) a nucleotide sequence described in SEQ ID NO:X or contained in the cDNA sequence of ATCC Deposit No:Z; (b) a nucleotide sequence in SEQ ID NO:X or the cDNA in ATCC Deposit No:Z which encodes the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in ATCC Deposit No:Z; (c) a nucleotide sequence in SEQ ID NO:X or the cDNA in ATCC Deposit No:Z which encodes a mature
30 polypeptide (i.e., a secreted polypeptide (e.g., as delineated in columns 14 and 15 of Table 1A)); (d) a nucleotide sequence in SEQ ID NO:X or the cDNA sequence of ATCC Deposit No:Z, which encodes a biologically active fragment of a polypeptide; (e) a nucleotide sequence in SEQ ID NO:X or the cDNA sequence of ATCC Deposit No:Z, which encodes an antigenic fragment of a polypeptide; (f) a nucleotide sequence encoding a polypeptide comprising the complete amino
35 acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in ATCC Deposit No:Z; (g) a nucleotide sequence encoding a mature polypeptide of the amino acid sequence of SEQ ID NO:Y (i.e., a secreted polypeptide (e.g., as delineated in columns 14 and 15

of Table 1A)) or a mature polypeptide of the amino acid sequence encoded by the cDNA in ATCC Deposit No:Z ; (h) a nucleotide sequence encoding a biologically active fragment of a polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in ATCC Deposit No:Z; (i) a nucleotide sequence encoding an antigenic
 5 fragment of a polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in ATCC Deposit No:Z; and (j) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), (h), or (i) above.

The present invention is also directed to nucleic acid molecules which comprise, or
 10 alternatively consist of, a nucleotide sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100%, identical to, for example, any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j) above, the nucleotide coding sequence in SEQ ID NO:X or the complementary strand thereto, the nucleotide coding sequence of the cDNA contained in ATCC Deposit No:Z or the complementary strand thereto, a nucleotide sequence encoding the
 15 polypeptide of SEQ ID NO:Y, a nucleotide sequence encoding a polypeptide sequence encoded by the nucleotide sequence in SEQ ID NO:X, a polypeptide sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X, a nucleotide sequence encoding the polypeptide encoded by the cDNA contained in ATCC Deposit No:Z, the nucleotide coding sequence in SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto, a
 20 nucleotide sequence encoding the polypeptide encoded by the nucleotide sequence in SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto, the nucleotide coding sequence in SEQ ID NO:B as defined in column 6 of Table 1C or the complementary strand thereto, a nucleotide sequence encoding the polypeptide encoded by the nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1C or the complementary
 25 strand thereto, the nucleotide sequence in SEQ ID NO:X encoding the polypeptide sequence as defined in columns 6 and 7 of Table 1B.1 or the complementary strand thereto, nucleotide sequences encoding the polypeptide as defined in column 6 and 7 of Table 1B.1 or the complementary strand thereto, and/or polynucleotide fragments of any of these nucleic acid molecules (e.g., those fragments described herein). Polynucleotides which hybridize to the
 30 complement of these nucleic acid molecules under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides and nucleic acids.

In a preferred embodiment, the invention encompasses nucleic acid molecules which comprise, or alternatively, consist of a polynucleotide which hybridizes under stringent
 35 hybridization conditions, or alternatively, under lower stringency conditions, to a polynucleotide in (a), (b), (c), (d), (e), (f), (g), (h), or (i), above, as are polypeptides encoded by these polynucleotides. In another preferred embodiment, polynucleotides which hybridize to the

complement of these nucleic acid molecules under stringent hybridization conditions, or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

In another embodiment, the invention provides a purified protein comprising, or
5 alternatively consisting of, a polypeptide having an amino acid sequence selected from the group consisting of: (a) the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in ATCC Deposit No:Z; (b) the amino acid sequence of a mature (secreted) form of a polypeptide having the amino acid sequence of SEQ ID NO:Y (e.g., as delineated in columns 14 and 15 of Table 1A) or a mature form of the amino acid sequence
10 encoded by the cDNA in ATCC Deposit No:Z mature; (c) the amino acid sequence of a biologically active fragment of a polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in ATCC Deposit No:Z; and (d) the amino acid sequence of an antigenic fragment of a polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in
15 ATCC Deposit No:Z.

The present invention is also directed to proteins which comprise, or alternatively consist of, an amino acid sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100%, identical to, for example, any of the amino acid sequences in (a), (b), (c), or (d), above, the amino acid sequence shown in SEQ ID NO:Y, the amino acid sequence encoded by the cDNA
20 contained in ATCC Deposit No:Z, the amino acid sequence of the polypeptide encoded by the nucleotide sequence in SEQ ID NO:X as defined in columns 8 and 9 of Table 2, the amino acid sequence of the polypeptide encoded by the nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1C, the amino acid sequence as defined in columns 6 and 7 of Table 1B.1, an amino acid sequence encoded by the nucleotide sequence in SEQ ID NO:X, and an amino acid
25 sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X. Fragments of these polypeptides are also provided (e.g., those fragments described herein). Further proteins encoded by polynucleotides which hybridize to the complement of the nucleic acid molecules encoding these amino acid sequences under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are the
30 polynucleotides encoding these proteins.

By a nucleic acid having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the nucleic acid is identical to the reference sequence except that the nucleotide sequence may include up to five point mutations per each 100 nucleotides of the reference nucleotide sequence
35 encoding the polypeptide. In other words, to obtain a nucleic acid having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to

5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be an entire sequence referred to in Table 1B or 2 as the ORF (open reading frame), or any fragment specified as described herein.

As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of the present invention can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. 6:237-245 (1990)). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be compared by converting U's to T's. The result of said global sequence alignment is expressed as percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identity are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, Window Size=500 or the length of the subject nucleotide sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for 5' and 3' truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

For example, a 90 base subject sequence is aligned to a 100 base query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignment of the first 10 bases at 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases were perfectly matched the final percent identity would be 90%. In another example, a 90 base subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that

there are no bases on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to be made for the purposes of the present invention.

By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

As a practical matter, whether any particular polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequence of a polypeptide referred to in Table 1A (e.g., the amino acid sequence delineated in columns 14 and 15) or a fragment thereof, Table 1B.1 (e.g., the amino acid sequence identified in column 6) or a fragment thereof, Table 2 (e.g., the amino acid sequence of the polypeptide encoded by the polynucleotide sequence defined in columns 8 and 9 of Table 2) or a fragment thereof, the amino acid sequence of the polypeptide encoded by the polynucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1C or a fragment thereof, the amino acid sequence of the polypeptide encoded by the nucleotide sequence in SEQ ID NO:X or a fragment thereof, or the amino acid sequence of the polypeptide encoded by cDNA contained in ATCC Deposit No:Z, or a fragment thereof, the amino acid sequence of a mature (secreted) polypeptide encoded by cDNA contained in ATCC Deposit No:Z, or a fragment thereof, can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci.6:237-245 (1990)). In a sequence alignment the query and subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is expressed as percent identity. Preferred parameters used in a FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject amino acid sequence,

whichever is shorter.

If the subject sequence is shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity. For subject sequences truncated at the N- and C-termini, relative to the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C-terminal residues of the subject sequence.

For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C- termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence. This time the deletions are internal deletions so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to be made for the purposes of the present invention.

The polynucleotide variants of the invention may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, polypeptide variants in which less than 50, less than 40, less than 30, less than 20, less than 10, or 5-50, 5-25, 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also

preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as *E. coli*).

5 Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985)). These allelic variants can vary at either the polynucleotide and/or polypeptide level and are included in the present invention. Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

10 Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, one or more amino acids can be deleted from the N-terminus or C-terminus of the polypeptide of the present invention without substantial loss of biological function. As an example, Ron et al. (*J. Biol. Chem.* 268: 2984-2988 (1993)) reported variant KGF proteins
15 having heparin binding activity even after deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., *J. Biotechnology* 7:199-216 (1988).)

Moreover, ample evidence demonstrates that variants often retain a biological activity
20 similar to that of the naturally occurring protein. For example, Gayle and coworkers (*J. Biol. Chem.* 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that "[m]ost of the
25 molecule could be altered with little effect on either [binding or biological activity]." In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

Furthermore, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other
30 biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and
35 otherwise known in the art.

Thus, the invention further includes polypeptide variants which show a biological or functional activity of the polypeptides of the invention (such as, for example, activity useful in

detecting, preventing, diagnosing, prognosticating, treating, and/or ameliorating cardiovascular disorders). Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as to have little effect on activity.

The present application is directed to nucleic acid molecules at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed herein, (e.g., encoding a polypeptide having the amino acid sequence of an N and/or C terminal deletion), irrespective of whether they encode a polypeptide having functional activity. This is because even where a particular nucleic acid molecule does not encode a polypeptide having functional activity, one of skill in the art would still know how to use the nucleic acid molecule, for instance, as a hybridization probe or a polymerase chain reaction (PCR) primer. Uses of the nucleic acid molecules of the present invention that do not encode a polypeptide having functional activity include, *inter alia*, (1) isolating a gene or allelic or splice variants thereof in a cDNA library; (2) *in situ* hybridization (e.g., "FISH") to metaphase chromosomal spreads to provide precise chromosomal location of the gene, as described in Verma et al., *Human Chromosomes: A Manual of Basic Techniques*, Pergamon Press, New York (1988); (3) Northern Blot analysis for detecting mRNA expression in specific tissues (e.g., normal or diseased tissues); and (4) *in situ* hybridization (e.g., histochemistry) for detecting mRNA expression in specific tissues (e.g., normal or diseased tissues).

Preferred, however, are nucleic acid molecules having sequences at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed herein, which do, in fact, encode a polypeptide having functional activity. By a polypeptide having "functional activity" is meant, a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein and/or a mature (secreted) protein of the invention. Such functional activities include, but are not limited to, biological activity (such as, for example, activity useful in detecting, preventing, diagnosing, prognosticating, treating, and/or ameliorating cancer and other hyperproliferative diseases and disorders), antigenicity (ability to bind, or compete with a polypeptide of the invention for binding, to an anti-polypeptide of the invention antibody), immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide of the invention.

The functional activity of the polypeptides, and fragments, variants and derivatives of the invention, can be assayed by various methods.

For example, in one embodiment where one is assaying for the ability to bind or compete with a full-length polypeptide of the present invention for binding to an anti-polypeptide antibody, various immunoassays known in the art can be used, including but not limited to, competitive and non-competitive assay systems using techniques such as radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel

diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels, for example), western blots, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, and immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

In another embodiment, where a ligand is identified, or the ability of a polypeptide fragment, variant or derivative of the invention to multimerize is being evaluated, binding can be assayed, e.g., by means well-known in the art, such as, for example, reducing and non-reducing gel chromatography, protein affinity chromatography, and affinity blotting. See generally, Phizicky et al., Microbiol. Rev. 59:94-123 (1995). In another embodiment, the ability of physiological correlates of a polypeptide of the present invention to bind to a substrate(s) of the polypeptide of the invention can be routinely assayed using techniques known in the art.

In addition, assays described herein (see Examples) and otherwise known in the art may routinely be applied to measure the ability of polypeptides of the present invention and fragments, variants and derivatives thereof to elicit polypeptide related biological activity (either *in vitro* or *in vivo*). Other methods will be known to the skilled artisan and are within the scope of the invention.

Of course, due to the degeneracy of the genetic code, one of ordinary skill in the art will immediately recognize that a large number of the nucleic acid molecules having a sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to, for example, the nucleic acid sequence of the cDNA contained in ATCC Deposit No:Z, the nucleic acid sequence referred to in Table 1B (SEQ ID NO:X), the nucleic acid sequence disclosed in Table 1A (e.g., the nucleic acid sequence delineated in columns 7 and 8), the nucleic acid sequence disclosed in Table 2 (e.g., the nucleic acid sequence delineated in columns 8 and 9) or fragments thereof, will encode polypeptides "having functional activity." In fact, since degenerate variants of any of these nucleotide sequences all encode the same polypeptide, in many instances, this will be clear to the skilled artisan even without performing the above described comparison assay. It will be further recognized in the art that, for such nucleic acid molecules that are not degenerate variants, a reasonable number will also encode a polypeptide having functional activity. This is because the skilled artisan is fully aware of amino acid substitutions that are either less likely or not likely to significantly effect protein function (e.g., replacing one aliphatic amino acid with a second aliphatic amino acid), as further described below.

For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," Science 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. See Cunningham and Wells, Science 244:1081-1085 (1989). The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly.

Besides conservative amino acid substitution, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitutions with one or more of the amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), (iv) fusion of the polypeptide with additional amino acids, such as, for example, an IgG Fc fusion region peptide, serum albumin (preferably human serum albumin) or a fragment thereof, or leader or secretory sequence, or a sequence facilitating purification, or (v) fusion of the polypeptide with another compound, such as albumin (including but not limited to recombinant albumin (see, e.g., U.S. Patent No. 5,876,969,

issued March 2, 1999, EP Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 16, 1998, herein incorporated by reference in their entirety)). Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. See Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).

10 A further embodiment of the invention relates to polypeptides which comprise the amino acid sequence of a polypeptide having an amino acid sequence which contains at least one amino acid substitution, but not more than 50 amino acid substitutions, even more preferably, not more than 40 amino acid substitutions, still more preferably, not more than 30 amino acid substitutions, and still even more preferably, not more than 20 amino acid substitutions from a polypeptide
15 sequence disclosed herein. Of course it is highly preferable for a polypeptide to have an amino acid sequence which, for example, comprises the amino acid sequence of a polypeptide of SEQ ID NO:Y, the amino acid sequence of the mature (e.g., secreted) polypeptide of SEQ ID NO:Y, an amino acid sequence encoded by SEQ ID NO:X, an amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, an amino acid sequence encoded by
20 the complement of SEQ ID NO:X, an amino acid sequence encoded by cDNA contained in ATCC Deposit No:Z, and/or the amino acid sequence of a mature (secreted) polypeptide encoded by cDNA contained in ATCC Deposit No:Z, or a fragment thereof, which contains, in order of ever-increasing preference, at least one, but not more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid substitutions.

25 In specific embodiments, the polypeptides of the invention comprise, or alternatively, consist of, fragments or variants of a reference amino acid sequence selected from: (a) the amino acid sequence of SEQ ID NO:Y or fragments thereof (e.g., the mature form and/or other fragments described herein); (b) the amino acid sequence encoded by SEQ ID NO:X or fragments thereof; (c) the amino acid sequence encoded by the complement of SEQ ID NO:X or fragments thereof;
30 (d) the amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or fragments thereof; and (e) the amino acid sequence encoded by cDNA contained in ATCC Deposit No:Z or fragments thereof; wherein the fragments or variants have 1-5, 5-10, 5-25, 5-50, 10-50 or 50-150, amino acid residue additions, substitutions, and/or deletions when compared to the reference amino acid sequence. In preferred embodiments, the amino acid
35 substitutions are conservative. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Polynucleotide and Polypeptide Fragments

The present invention is also directed to polynucleotide fragments of the polynucleotides (nucleic acids) of the invention. In the present invention, a "polynucleotide fragment" refers to a polynucleotide having a nucleic acid sequence which, for example: is a portion of the cDNA
 5 contained in ATCC Deposit No:Z or the complementary strand thereto; is a portion of the polynucleotide sequence encoding the polypeptide encoded by the cDNA contained in ATCC Deposit No:Z or the complementary strand thereto; is a portion of the polynucleotide sequence encoding the mature (secreted) polypeptide encoded by the cDNA contained in ATCC Deposit No:Z or the complementary strand thereto; is a portion of a polynucleotide sequence encoding the
 10 mature amino acid sequence as defined in columns 14 and 15 of Table 1A or the complementary strand thereto; is a portion of a polynucleotide sequence encoding the amino acid sequence encoded by the region of SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto; is a portion of the polynucleotide sequence of SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto; is a portion of the
 15 polynucleotide sequence in SEQ ID NO:X or the complementary strand thereto; is a polynucleotide sequence encoding a portion of the polypeptide of SEQ ID NO:Y; is a polynucleotide sequence encoding a portion of a polypeptide encoded by SEQ ID NO:X; is a polynucleotide sequence encoding a portion of a polypeptide encoded by the complement of the polynucleotide sequence in SEQ ID NO:X; is a portion of a polynucleotide sequence encoding the
 20 amino acid sequence encoded by the region of SEQ ID NO:B as defined in column 6 of Table 1C or the complementary strand thereto; or is a portion of the polynucleotide sequence of SEQ ID NO:B as defined in column 6 of Table 1C or the complementary strand thereto.

The polynucleotide fragments of the invention are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more
 25 preferably, at least about 40 nt, at least about 50 nt, at least about 75 nt, or at least about 150 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from the cDNA sequence contained in ATCC Deposit No:Z, or the nucleotide sequence shown in SEQ ID NO:X or the complementary strand thereto. In this context "about" includes the particularly recited value or a value larger or smaller by several (5, 4, 3, 2, or 1)
 30 nucleotides, at either terminus or at both termini. These nucleotide fragments have uses that include, but are not limited to, as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., at least 160, 170, 180, 190, 200, 250, 500, 600, 1000, or 2000 nucleotides in length) are also encompassed by the invention.

Moreover, representative examples of polynucleotide fragments of the invention comprise,
 35 or alternatively consist of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 601-650, 651-700, 701-750, 751-800, 801-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-

1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, 3551-3600, 3601-3650, 3651-3700, 3701-3750, 3751-3800, 3801-3850, 3851-3900, 3901-3950, 3951-4000, 4001-4050, 4051-4100, 4101-4150, 4151-4200, 4201-4250, 4251-4300, 4301-4350, 4351-4400, 4401-4450, 4451-4500, 4501-4550, 4551-4600, 4601-4650, 4651-4700, 4701-4750, 4751-4800, 4801-4850, 4851-4900, 4901-4950, 4951-5000, 5001-5050, 5051-5100, 5101-5150, 5151-5200, 5201-5250, 5251-5300, 5301-5350, 5351-5400, 5401-5450, 5451-5500, 5501-5550, 5551-5600, 5601-5650, 5651-5700, 5701-5750, 5751-5800, 5801-5850, 5851-5900, 5901-5950, 5951-6000, 6001-6050, 6051-6100, 6101-6150, 6151-6200, 6201-6250, 6251-6300, 6301-6350, 6351-6400, 6401-6450, 6451-6500, 6501-6550, 6551-6600, 6601-6650, 6651-6700, 6701-6750, 6751-6800, 6801-6850, 6851-6900, 6901-6950, 6951-7000, 7001-7050, 7051-7100, 7101-7150, 7151-7200, 7201-7250, 7251-7300 or 7301 to the end of SEQ ID NO:X, or the complementary strand thereto. In this context "about" includes the particularly recited range or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a functional activity (e.g., biological activity; such as, for example, activity useful in detecting, preventing, diagnosing, prognosticating, treating, and/or ameliorating cancer and other hyperproliferative diseases and disorders). More preferably, these polynucleotides can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

Further representative examples of polynucleotide fragments of the invention comprise, or alternatively consist of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 601-650, 651-700, 701-750, 751-800, 801-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, 3551-3600, 3601-3650, 3651-3700, 3701-3750, 3751-3800, 3801-3850, 3851-3900, 3901-3950, 3951-4000, 4001-4050, 4051-4100, 4101-4150, 4151-4200, 4201-4250, 4251-4300, 4301-

4350, 4351-4400, 4401-4450, 4451-4500, 4501-4550, 4551-4600, 4601-4650, 4651-4700, 4701-4750, 4751-4800, 4801-4850, 4851-4900, 4901-4950, 4951-5000, 5001-5050, 5051-5100, 5101-5150, 5151-5200, 5201-5250, 5251-5300, 5301-5350, 5351-5400, 5401-5450, 5451-5500, 5501-5550, 5551-5600, 5601-5650, 5651-5700, 5701-5750, 5751-5800, 5801-5850, 5851-5900, 5901-5950, 5951-6000, 6001-6050, 6051-6100, 6101-6150, 6151-6200, 6201-6250, 6251-6300, 6301-6350, 6351-6400, 6401-6450, 6451-6500, 6501-6550, 6551-6600, 6601-6650, 6651-6700, 6701-6750, 6751-6800, 6801-6850, 6851-6900, 6901-6950, 6951-7000, 7001-7050, 7051-7100, 7101-7150, 7151-7200, 7201-7250, 7251-7300 or 7301 to the end of the cDNA sequence contained in ATCC Deposit No:Z, or the complementary strand thereto. In this context "about" includes the particularly recited range or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a functional activity (e.g., biological activity). More preferably, these polynucleotides can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

Moreover, representative examples of polynucleotide fragments of the invention comprise, or alternatively consist of, a nucleic acid sequence comprising one, two, three, four, five, six, seven, eight, nine, ten, or more of the above described polynucleotide fragments of the invention in combination with a polynucleotide sequence delineated in Table 1C column 6. Additional, representative examples of polynucleotide fragments of the invention comprise, or alternatively consist of, a nucleic acid sequence comprising one, two, three, four, five, six, seven, eight, nine, ten, or more of the above described polynucleotide fragments of the invention in combination with a polynucleotide sequence that is the complementary strand of a sequence delineated in column 6 of Table 1C. In further embodiments, the above-described polynucleotide fragments of the invention comprise, or alternatively consist of, sequences delineated in Table 1C, column 6, and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1C, column 5). In additional embodiments, the above-described polynucleotide fragments of the invention comprise, or alternatively consist of, sequences delineated in Table 1C, column 6, and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated Table 1C, column 6, and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by

the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more fragments of the sequences delineated in column 6 of Table 1C, and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1C, column 2) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more fragments of the sequences delineated in column 6 of Table 1C which correspond to the same ATCC Deposit No:Z (see Table 1C, column 1), and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A, 1B, or 1C) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more fragments of the sequences delineated in the same row of column 6 of Table 1C, and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A, 1B, or 1C) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C and the 5' 10 polynucleotides of the sequence of SEQ ID NO:X are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C and the 5' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X (e.g., as described herein) are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also

encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X and the 5' 10 polynucleotides of the sequence of one of the sequences delineated in column 6 of Table 1C are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C and the 5' 10 polynucleotides of another sequence in column 6 are directly contiguous. In preferred embodiments, the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C is directly contiguous with the 5' 10 polynucleotides of the next sequential exon delineated in Table 1C, column 6. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

In the present invention, a "polypeptide fragment" refers to an amino acid sequence which is a portion of the amino acid sequence contained in SEQ ID NO:Y, is a portion of the mature form of SEQ ID NO:Y as defined in columns 14 and 15 of Table 1A, a portion of an amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, is a portion of an amino acid sequence encoded by the polynucleotide sequence of SEQ ID NO:X, is a portion of an amino acid sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X, is a portion of the amino acid sequence of a mature (secreted) polypeptide encoded by the cDNA contained in ATCC Deposit No:Z, and/or is a portion of an amino acid sequence

encoded by the cDNA contained in ATCC Deposit No:Z. Protein (polypeptide) fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 101-120, 121-140, 141-160, 161-180, 181-200, 201-220, 221-240, 241-260, 261-280, 281-300, 301-320, 321-340, 341-360, 361-380, 381-400, 401-420, 421-440, 441-460, 461-480, 481-500, 501-520, 521-540, 541-560, 561-580, 581-600, 601-620, 621-640, 641-660, 661-680, 681-700, 701-720, 721-740, 741-760, 761-780, 781-800, 801-820, 821-840, 841-860, 861-880, 881-900, 901-920, 921-940, 941-960, 961-980, 981-1000, 1001-1020, 1021-1040, 1041-1060, 1061-1080, 1081-1100, 1101-1120, 1121-1140, 1141-1160, 1161-1180, 1181-1200, 1201-1220, 1221-1240, 1241-1260, 1261-1280, 1281-1300, 1301-1320, 1321-1340, 1341-1360, 1361-1380, 1381-1400, 1401-1420, 1421-1440, or 1441 to the end of the coding region of cDNA and SEQ ID NO: Y. In a preferred embodiment, polypeptide fragments of the invention include, for example, fragments comprising, or alternatively consisting of, from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 101-120, 121-140, 141-160, 161-180, 181-200, 201-220, 221-240, 241-260, 261-280, 281-300, 301-320, 321-340, 341-360, 361-380, 381-400, 401-420, 421-440, 441-460, 461-480, 481-500, 501-520, 521-540, 541-560, 561-580, 581-600, 601-620, 621-640, 641-660, 661-680, 681-700, 701-720, 721-740, 741-760, 761-780, 781-800, 801-820, 821-840, 841-860, 861-880, 881-900, 901-920, 921-940, 941-960, 961-980, 981-1000, 1001-1020, 1021-1040, 1041-1060, 1061-1080, 1081-1100, 1101-1120, 1121-1140, 1141-1160, 1161-1180, 1181-1200, 1201-1220, 1221-1240, 1241-1260, 1261-1280, 1281-1300, 1301-1320, 1321-1340, 1341-1360, 1361-1380, 1381-1400, 1401-1420, 1421-1440, or 1441 to the end of the coding region of SEQ ID NO:Y. Moreover, polypeptide fragments of the invention may be at least about 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges or values, or ranges or values larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes. Polynucleotides encoding these polypeptide fragments are also encompassed by the invention.

Even if deletion of one or more amino acids from the N-terminus of a protein results in modification or loss of one or more biological functions of the protein, other functional activities (e.g., biological activities; such as, for example, activity useful in detecting, preventing, diagnosing, prognosticating, treating, and/or ameliorating cancer and other hyperproliferative diseases and disorders; ability to multimerize; ability to bind a ligand; antigenic ability useful for production of polypeptide specific antibodies) may still be retained. For example, the ability of shortened muteins to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptides generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the N-terminus. Whether a particular

polypeptide lacking N-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a mutein with a large number of deleted N-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

Accordingly, polypeptide fragments include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above amino and carboxy terminus deletions are preferred. Similarly, polynucleotides encoding these polypeptide fragments are also preferred.

The present invention further provides polypeptides having one or more residues deleted from the amino terminus of the amino acid sequence of a polypeptide disclosed herein (e.g., a polypeptide of SEQ ID NO:Y, a polypeptide as defined in columns 14 and 15 of Table 1A, a polypeptide encoded by the polynucleotide sequence contained in SEQ ID NO:X or the complement thereof, a polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, a polypeptide encoded by the portion of SEQ ID NO:B as defined in column 6 of Table 1C, a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z, and/or a mature polypeptide encoded by the cDNA contained in ATCC Deposit No:Z). In particular, N-terminal deletions may be described by the general formula m-q, where q is a whole integer representing the total number of amino acid residues in a polypeptide of the invention (e.g., the polypeptide disclosed in SEQ ID NO:Y, the mature (secreted) portion of SEQ ID NO:Y as defined in columns 14 and 15 of Table 1A, or the polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2), and m is defined as any integer ranging from 2 to q-6. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The present invention further provides polypeptides having one or more residues from the carboxy terminus of the amino acid sequence of a polypeptide disclosed herein (e.g., a polypeptide of SEQ ID NO:Y, the mature (secreted) portion of SEQ ID NO:Y as defined in columns 14 and 15 of Table 1A, a polypeptide encoded by the polynucleotide sequence contained in SEQ ID NO:X, a polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, a polypeptide encoded by the portion of SEQ ID NO:B as defined in column 6 of Table 1C, a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z, and/or a mature polypeptide encoded by the cDNA contained in ATCC Deposit No:Z). In particular, C-terminal deletions may be described by the general formula 1-n, where n is any whole integer ranging from 6 to q-1, and

where n corresponds to the position of amino acid residue in a polypeptide of the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

In addition, any of the above described N- or C-terminal deletions can be combined to produce a N- and C-terminal deleted polypeptide. The invention also provides polypeptides
5 having one or more amino acids deleted from both the amino and the carboxyl termini, which may be described generally as having residues m-n of a polypeptide encoded by SEQ ID NO:X (e.g., including, but not limited to, the preferred polypeptide disclosed as SEQ ID NO:Y, the mature (secreted) portion of SEQ ID NO:Y as defined in columns 14 and 15 of Table 1A, and the polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2),
10 the cDNA contained in ATCC Deposit No:Z, and/or the complement thereof, where n and m are integers as described above. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Also as mentioned above, even if deletion of one or more amino acids from the C-terminus of a protein results in modification of loss of one or more biological functions of the
15 protein, other functional activities (e.g., biological activities such as, for example, activity useful in detecting, preventing, diagnosing, prognosticating, treating, and/or ameliorating cancer and other hyperproliferative diseases and disorders; ability to multimerize; ability to bind a ligand; antigenic ability useful for production of polypeptide specific antibodies) may still be retained. For example the ability of the shortened mutein to induce and/or bind to antibodies which recognize the
20 complete or mature forms of the polypeptide generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the C-terminus. Whether a particular polypeptide lacking C-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a mutein with a large number of deleted
25 C-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

The present application is also directed to proteins containing polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a polypeptide sequence set forth herein. In preferred embodiments, the application is directed to proteins containing polypeptides at least
30 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to polypeptides having the amino acid sequence of the specific N- and C-terminal deletions. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Any polypeptide sequence encoded by, for example, the polynucleotide sequences set forth as SEQ ID NO:X or the complement thereof, (presented, for example, in Tables 1A and 2),
35 the cDNA contained in ATCC Deposit No:Z, or the polynucleotide sequence as defined in column 6 of Table 1C, may be analyzed to determine certain preferred regions of the polypeptide. For example, the amino acid sequence of a polypeptide encoded by a polynucleotide sequence of SEQ

ID NO:X (e.g., the polypeptide of SEQ ID NO:Y and the polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2) or the cDNA contained in ATCC Deposit No:Z may be analyzed using the default parameters of the DNASTAR computer algorithm (DNASTAR, Inc., 1228 S. Park St., Madison, WI 53715 USA; <http://www.dnastar.com/>).

Polypeptide regions that may be routinely obtained using the DNASTAR computer algorithm include, but are not limited to, Garnier-Robson alpha-regions, beta-regions, turn-regions, and coil-regions; Chou-Fasman alpha-regions, beta-regions, and turn-regions; Kyte-Doolittle hydrophilic regions and hydrophobic regions; Eisenberg alpha- and beta-amphipathic regions; Karplus-Schulz flexible regions; Emini surface-forming regions; and Jameson-Wolf regions of high antigenic index. Among highly preferred polynucleotides of the invention in this regard are those that encode polypeptides comprising regions that combine several structural features, such as several (e.g., 1, 2, 3 or 4) of the features set out above.

Additionally, Kyte-Doolittle hydrophilic regions and hydrophobic regions, Emini surface-forming regions, and Jameson-Wolf regions of high antigenic index (i.e., containing four or more contiguous amino acids having an antigenic index of greater than or equal to 1.5, as identified using the default parameters of the Jameson-Wolf program) can routinely be used to determine polypeptide regions that exhibit a high degree of potential for antigenicity. Regions of high antigenicity are determined from data by DNASTAR analysis by choosing values which represent regions of the polypeptide which are likely to be exposed on the surface of the polypeptide in an environment in which antigen recognition may occur in the process of initiation of an immune response.

Preferred polypeptide fragments of the invention are fragments comprising, or alternatively, consisting of, an amino acid sequence that displays a functional activity (e.g. biological activity such as, for example, activity useful in detecting, preventing, diagnosing, prognosticating, treating, and/or ameliorating cancer and other hyperproliferative diseases and disorders; ability to multimerize; ability to bind a ligand; antigenic ability useful for production of polypeptide specific antibodies) of the polypeptide sequence of which the amino acid sequence is a fragment. By a polypeptide displaying a "functional activity" is meant a polypeptide capable of one or more known functional activities associated with a full-length protein, such as, for example, biological activity, antigenicity, immunogenicity, and/or multimerization, as described herein.

Other preferred polypeptide fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

In preferred embodiments, polypeptides of the invention comprise, or alternatively consist of, one, two, three, four, five or more of the antigenic fragments of the polypeptide of SEQ ID

NO:Y, or portions thereof. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Epitopes and Antibodies

5 The present invention encompasses polypeptides comprising, or alternatively consisting of, an epitope of: the polypeptide sequence shown in SEQ ID NO:Y; a polypeptide sequence encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2; the polypeptide sequence encoded by the portion of SEQ ID NO:B as defined in column 6 of Table 1C
10 or the complement thereto; the polypeptide sequence encoded by the cDNA contained in ATCC Deposit No:Z; or the polypeptide sequence encoded by a polynucleotide that hybridizes to the sequence of SEQ ID NO:X, the complement of the sequence of SEQ ID NO:X, the complement of a portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, or the cDNA sequence contained in ATCC Deposit No:Z under stringent hybridization conditions or alternatively, under
15 lower stringency hybridization as defined *supra*. The present invention further encompasses polynucleotide sequences encoding an epitope of a polypeptide sequence of the invention (such as, for example, the sequence disclosed in SEQ ID NO:X, or a fragment thereof), polynucleotide sequences of the complementary strand of a polynucleotide sequence encoding an epitope of the invention, and polynucleotide sequences which hybridize to the complementary strand under
20 stringent hybridization conditions or alternatively, under lower stringency hybridization conditions defined *supra*.

 The term "epitopes," as used herein, refers to portions of a polypeptide having antigenic or immunogenic activity in an animal, preferably a mammal, and most preferably in a human. In a preferred embodiment, the present invention encompasses a polypeptide comprising an epitope,
25 as well as the polynucleotide encoding this polypeptide. An "immunogenic epitope," as used herein, is defined as a portion of a protein that elicits an antibody response in an animal, as determined by any method known in the art, for example, by the methods for generating antibodies described *infra*. (See, for example, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998-4002 (1983)). The term "antigenic epitope," as used herein, is defined as a portion of a protein to
30 which an antibody can immunospecifically bind its antigen as determined by any method well known in the art, for example, by the immunoassays described herein. Immunospecific binding excludes non-specific binding but does not necessarily exclude cross-reactivity with other antigens. Antigenic epitopes need not necessarily be immunogenic.

 Fragments which function as epitopes may be produced by any conventional means. (See,
35 e.g., Houghten, R. A., Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985) further described in U.S. Patent No. 4,631,211.)

In the present invention, antigenic epitopes preferably contain a sequence of at least 4, at least 5, at least 6, at least 7, more preferably at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, and, most preferably, between about 15 to about 30 amino acids. Preferred polypeptides comprising
5 immunogenic or antigenic epitopes are at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 amino acid residues in length. Additional non-exclusive preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as portions thereof. Antigenic epitopes are useful, for example, to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. Preferred antigenic epitopes include the antigenic epitopes disclosed
10 herein, as well as any combination of two, three, four, five or more of these antigenic epitopes. Antigenic epitopes can be used as the target molecules in immunoassays. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe et al., Science 219:660-666 (1983)).

Non-limiting examples of epitopes of polypeptides that can be used to generate antibodies of the invention include a polypeptide comprising, or alternatively consisting of, at least one, two,
15 three, four, five, six or more of the portion(s) of SEQ ID NO:Y specified in column 6 of Table 1B.1. These polypeptide fragments have been determined to bear antigenic epitopes of the proteins of the invention by the analysis of the Jameson-Wolf antigenic index which is included in the DNASTar suite of computer programs. By "comprise" it is intended that a polypeptide contains at least one, two, three, four, five, six or more of the portion(s) of SEQ ID NO:Y shown in column
20 6 of Table 1B.1, but it may contain additional flanking residues on either the amino or carboxyl termini of the recited portion. Such additional flanking sequences are preferably sequences naturally found adjacent to the portion; i.e., contiguous sequence shown in SEQ ID NO:Y. The flanking sequence may, however, be sequences from a heterologous polypeptide, such as from another protein described herein or from a heterologous polypeptide not described herein. In
25 particular embodiments, epitope portions of a polypeptide of the invention comprise one, two, three, or more of the portions of SEQ ID NO:Y shown in column 6 of Table 1B.1.

Similarly, immunogenic epitopes can be used, for example, to induce antibodies according to methods well known in the art. See, for instance, Sutcliffe et al., *supra*; Wilson et al., *supra*; Chow et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle et al., J. Gen. Virol.
30 66:2347-2354 (1985). Preferred immunogenic epitopes include the immunogenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these immunogenic epitopes. The polypeptides comprising one or more immunogenic epitopes may be presented for eliciting an antibody response together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse), or, if the polypeptide is of sufficient length (at least
35 about 25 amino acids), the polypeptide may be presented without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient

to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting).

Epitope-bearing polypeptides of the present invention may be used to induce antibodies according to methods well known in the art including, but not limited to, *in vivo* immunization, *in vitro* immunization, and phage display methods. See, e.g., Sutcliffe et al., *supra*; Wilson et al., *supra*, and Bittle et al., J. Gen. Virol., 66:2347-2354 (1985). If *in vivo* immunization is used, animals may be immunized with free peptide; however, anti-peptide antibody titer may be boosted by coupling the peptide to a macromolecular carrier, such as keyhole limpet hemacyanin (KLH) or tetanus toxoid. For instance, peptides containing cysteine residues may be coupled to a carrier using a linker such as maleimidobenzoyl- N-hydroxysuccinimide ester (MBS), while other peptides may be coupled to carriers using a more general linking agent such as glutaraldehyde. Animals such as rabbits, rats and mice are immunized with either free or carrier- coupled peptides, for instance, by intraperitoneal and/or intradermal injection of emulsions containing about 100 μ g of peptide or carrier protein and Freund's adjuvant or any other adjuvant known for stimulating an immune response. Several booster injections may be needed, for instance, at intervals of about two weeks, to provide a useful titer of anti-peptide antibody which can be detected, for example, by ELISA assay using free peptide adsorbed to a solid surface. The titer of anti-peptide antibodies in serum from an immunized animal may be increased by selection of anti-peptide antibodies, for instance, by adsorption to the peptide on a solid support and elution of the selected antibodies according to methods well known in the art.

As one of skill in the art will appreciate, and as discussed above, the polypeptides of the present invention (e.g., those comprising an immunogenic or antigenic epitope) can be fused to heterologous polypeptide sequences. For example, polypeptides of the present invention (including fragments or variants thereof), may be fused with the constant domain of immunoglobulins (IgA, IgE, IgG, IgM), or portions thereof (CH1, CH2, CH3, or any combination thereof and portions thereof, resulting in chimeric polypeptides. By way of another non-limiting example, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) may be fused with albumin (including but not limited to recombinant human serum albumin or fragments or variants thereof (see, e.g., U.S. Patent No. 5,876,969, issued March 2, 1999, EP Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 16, 1998, herein incorporated by reference in their entirety)). In a preferred embodiment, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) are fused with the mature form of human serum albumin (i.e., amino acids 1 – 585 of human serum albumin as shown in Figures 1 and 2 of EP Patent 0 322 094) which is herein incorporated by reference in its entirety. In another preferred embodiment, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) are fused with polypeptide fragments comprising, or alternatively consisting of, amino acid residues 1-z of human serum albumin, where z is an integer

from 369 to 419, as described in U.S. Patent 5,766,883 herein incorporated by reference in its entirety. Polypeptides and/or antibodies of the present invention (including fragments or variants thereof) may be fused to either the N- or C-terminal end of the heterologous protein (e.g., immunoglobulin Fc polypeptide or human serum albumin polypeptide). Polynucleotides encoding fusion proteins of the invention are also encompassed by the invention.

Such fusion proteins as those described above may facilitate purification and may increase half-life *in vivo*. This has been shown for chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. See, e.g., EP 394,827; Traunecker et al., *Nature*, 331:84-86 (1988). Enhanced delivery of an antigen across the epithelial barrier to the immune system has been demonstrated for antigens (e.g., insulin) conjugated to an FcRn binding partner such as IgG or Fc fragments (see, e.g., PCT Publications WO 96/22024 and WO 99/04813). IgG fusion proteins that have a disulfide-linked dimeric structure due to the IgG portion disulfide bonds have also been found to be more efficient in binding and neutralizing other molecules than monomeric polypeptides or fragments thereof alone. See, e.g., Fountoulakis et al., *J. Biochem.*, 270:3958-3964 (1995). Nucleic acids encoding the above epitopes can also be recombined with a gene of interest as an epitope tag (e.g., the hemagglutinin (HA) tag or flag tag) to aid in detection and purification of the expressed polypeptide. For example, a system described by Janknecht et al. allows for the ready purification of non-denatured fusion proteins expressed in human cell lines (Janknecht et al., 1991, *Proc. Natl. Acad. Sci. USA* 88:8972- 897). In this system, the gene of interest is subcloned into a vaccinia recombination plasmid such that the open reading frame of the gene is translationally fused to an amino-terminal tag consisting of six histidine residues. The tag serves as a matrix binding domain for the fusion protein. Extracts from cells infected with the recombinant vaccinia virus are loaded onto Ni²⁺ nitriloacetic acid-agarose column and histidine-tagged proteins can be selectively eluted with imidazole-containing buffers.

Fusion Proteins

Any polypeptide of the present invention can be used to generate fusion proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the polypeptide of the present invention can be used to indirectly detect the second protein by binding to the polypeptide. Moreover, because secreted proteins target cellular locations based on trafficking signals, polypeptides of the present invention which are shown to be secreted can be used as targeting molecules once fused to other proteins.

Examples of domains that can be fused to polypeptides of the present invention include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

In certain preferred embodiments, proteins of the invention are fusion proteins comprising

an amino acid sequence that is an N and/or C- terminal deletion of a polypeptide of the invention. In preferred embodiments, the invention is directed to a fusion protein comprising an amino acid sequence that is at least 90%, 95%, 96%, 97%, 98% or 99% identical to a polypeptide sequence of the invention. Polynucleotides encoding these proteins are also encompassed by the invention.

5 Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell or subsequent handling and storage. Also, peptide moieties may be added to the polypeptide to facilitate purification. Such regions may be
10 removed prior to final preparation of the polypeptide. The addition of peptide moieties to facilitate handling of polypeptides are familiar and routine techniques in the art.

 As one of skill in the art will appreciate that, as discussed above, polypeptides of the present invention, and epitope-bearing fragments thereof, can be combined with heterologous polypeptide sequences. For example, the polypeptides of the present invention may be fused with
15 heterologous polypeptide sequences, for example, the polypeptides of the present invention may be fused with the constant domain of immunoglobulins (IgA, IgE, IgG, IgM) or portions thereof (CH1, CH2, CH3, and any combination thereof, including both entire domains and portions thereof), or albumin (including, but not limited to, native or recombinant human albumin or fragments or variants thereof (see, e.g., U.S. Patent No. 5,876,969, issued March 2, 1999, EP
20 Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 16, 1998, herein incorporated by reference in their entirety)), resulting in chimeric polypeptides. For example, EP-A-O 464 533 (Canadian counterpart 2045869) discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can
25 result in, for example, improved pharmacokinetic properties (EP-A 0232 262). Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to
30 identify antagonists of hIL-5. See, D. Bennett et al., J. Molecular Recognition 8:52-58 (1995); K. Johanson et al., J. Biol. Chem. 270:9459-9471 (1995).

 Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a polypeptide which facilitates purification of the fused polypeptide. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided
35 in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the

fusion protein. Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., Cell 37:767 (1984)).

Additional fusion proteins of the invention may be generated through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling"). DNA shuffling may be employed to modulate the activities of polypeptides of the invention, such methods can be used to generate polypeptides with altered activity, as well as agonists and antagonists of the polypeptides. See, generally, U.S. Patent Nos. 5,605,793; 5,811,238; 5,830,721; 5,834,252; and 5,837,458, and Patten et al., Curr. Opinion Biotechnol. 8:724-33 (1997); Harayama, Trends Biotechnol. 16(2):76-82 (1998); Hansson, et al., J. Mol. Biol. 287:265-76 (1999); and Lorenzo and Blasco, Biotechniques 24(2):308- 13 (1998) (each of these patents and publications are hereby incorporated by reference in its entirety). In one embodiment, alteration of polynucleotides corresponding to SEQ ID NO:X and the polypeptides encoded by these polynucleotides may be achieved by DNA shuffling. DNA shuffling involves the assembly of two or more DNA segments by homologous or site-specific recombination to generate variation in the polynucleotide sequence. In another embodiment, polynucleotides of the invention, or the encoded polypeptides, may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of a polynucleotide encoding a polypeptide of the invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules.

Thus, any of these above fusions can be engineered using the polynucleotides or the polypeptides of the present invention.

Recombinant and Synthetic Production of Polypeptides of the Invention

The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by synthetic and recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or retroviral vector. Retroviral vectors may be replication competent or replication defective. In the latter case, viral propagation generally will occur only in complementing host cells.

The polynucleotides of the invention may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the vector is a virus, it may be packaged in vitro using an appropriate packaging cell line and then transduced into host cells.

The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the E. coli lac, trp, phoA and tac promoters, the SV40 early and

late promoters and promoters of retroviral LTRs, to name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a translation
5 initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418, glutamine synthase, or neomycin resistance for eukaryotic cell culture, and tetracycline, kanamycin or ampicillin resistance genes for culturing
10 in *E. coli* and other bacteria. Representative examples of appropriate hosts include, but are not limited to, bacterial cells, such as *E. coli*, *Streptomyces* and *Salmonella typhimurium* cells; fungal cells, such as yeast cells (e.g., *Saccharomyces cerevisiae* or *Pichia pastoris* (ATCC Accession No. 201178)); insect cells such as *Drosophila* S2 and *Spodoptera Sf9* cells; animal cells such as CHO, COS, 293, and Bowes melanoma cells; and plant cells. Appropriate culture mediums and
15 conditions for the above-described host cells are known in the art.

Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors, Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 available from Pharmacia Biotech, Inc. Among preferred eukaryotic vectors are
20 pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; and pSVK3, pBPV, pMSG and pSVL available from Pharmacia. Preferred expression vectors for use in yeast systems include, but are not limited to pYES2, pYD1, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalph, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, pPIC9K, and PAO815 (all available from Invitrogen, Carlsbad, CA). Other suitable vectors will be readily apparent to the skilled
25 artisan.

Vectors which use glutamine synthase (GS) or DHFR as the selectable markers can be amplified in the presence of the drugs methionine sulfoximine or methotrexate, respectively. An advantage of glutamine synthase based vectors are the availability of cell lines (e.g., the murine myeloma cell line, NS0) which are glutamine synthase negative. Glutamine synthase expression
30 systems can also function in glutamine synthase expressing cells (e.g., Chinese Hamster Ovary (CHO) cells) by providing additional inhibitor to prevent the functioning of the endogenous gene. A glutamine synthase expression system and components thereof are detailed in PCT publications: WO87/04462; WO86/05807; WO89/01036; WO89/10404; and WO91/06657, which are hereby incorporated in their entireties by reference herein. Additionally, glutamine synthase expression
35 vectors can be obtained from Lonza Biologics, Inc. (Portsmouth, NH). Expression and production of monoclonal antibodies using a GS expression system in murine myeloma cells is described in

Bebbington *et al.*, *Bio/technology* 10:169(1992) and in Biblia and Robinson *Biotechnol. Prog.* 11:1 (1995) which are herein incorporated by reference.

The present invention also relates to host cells containing the above-described vector constructs described herein, and additionally encompasses host cells containing nucleotide sequences of the invention that are operably associated with one or more heterologous control regions (e.g., promoter and/or enhancer) using techniques known of in the art. The host cell can be a higher eukaryotic cell, such as a mammalian cell (e.g., a human derived cell), or a lower eukaryotic cell, such as a yeast cell, or the host cell can be a prokaryotic cell, such as a bacterial cell. A host strain may be chosen which modulates the expression of the inserted gene sequences, or modifies and processes the gene product in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus expression of the genetically engineered polypeptide may be controlled. Furthermore, different host cells have characteristics and specific mechanisms for the translational and post-translational processing and modification (e.g., phosphorylation, cleavage) of proteins. Appropriate cell lines can be chosen to ensure the desired modifications and processing of the foreign protein expressed.

Introduction of the nucleic acids and nucleic acid constructs of the invention into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in many standard laboratory manuals, such as Davis *et al.*, *Basic Methods In Molecular Biology* (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

In addition to encompassing host cells containing the vector constructs discussed herein, the invention also encompasses primary, secondary, and immortalized host cells of vertebrate origin, particularly mammalian origin, that have been engineered to delete or replace endogenous genetic material (e.g., the coding sequence), and/or to include genetic material (e.g., heterologous polynucleotide sequences) that is operably associated with polynucleotides of the invention, and which activates, alters, and/or amplifies endogenous polynucleotides. For example, techniques known in the art may be used to operably associate heterologous control regions (e.g., promoter and/or enhancer) and endogenous polynucleotide sequences via homologous recombination (see, e.g., US Patent Number 5,641,670, issued June 24, 1997; International Publication Number WO 96/29411; International Publication Number WO 94/12650; Koller *et al.*, *Proc. Natl. Acad. Sci. USA* 86:8932-8935 (1989); and Zijlstra *et al.*, *Nature* 342:435-438 (1989), the disclosures of each of which are incorporated by reference in their entireties).

Polypeptides of the invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite

chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") is employed for purification.

Polypeptides of the present invention can also be recovered from: products purified from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells. Depending upon the host employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition, polypeptides of the invention may also include an initial modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient, depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

In one embodiment, the yeast *Pichia pastoris* is used to express polypeptides of the invention in a eukaryotic system. *Pichia pastoris* is a methylotrophic yeast which can metabolize methanol as its sole carbon source. A main step in the methanol metabolism pathway is the oxidation of methanol to formaldehyde using O₂. This reaction is catalyzed by the enzyme alcohol oxidase. In order to metabolize methanol as its sole carbon source, *Pichia pastoris* must generate high levels of alcohol oxidase due, in part, to the relatively low affinity of alcohol oxidase for O₂. Consequently, in a growth medium depending on methanol as a main carbon source, the promoter region of one of the two alcohol oxidase genes (*AOX1*) is highly active. In the presence of methanol, alcohol oxidase produced from the *AOX1* gene comprises up to approximately 30% of the total soluble protein in *Pichia pastoris*. See Ellis, S.B., *et al.*, *Mol. Cell. Biol.* 5:1111-21 (1985); Koutz, P.J., *et al.*, *Yeast* 5:167-77 (1989); Tschopp, J.F., *et al.*, *Nucl. Acids Res.* 15:3859-76 (1987). Thus, a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, under the transcriptional regulation of all or part of the *AOX1* regulatory sequence is expressed at exceptionally high levels in *Pichia* yeast grown in the presence of methanol.

In one example, the plasmid vector pPIC9K is used to express DNA encoding a polypeptide of the invention, as set forth herein, in a *Pichea* yeast system essentially as described in "Pichia Protocols: Methods in Molecular Biology," D.R. Higgins and J. Cregg, eds. The Humana Press, Totowa, NJ, 1998. This expression vector allows expression and secretion of a polypeptide of the invention by virtue of the strong *AOX1* promoter linked to the *Pichia pastoris*

alkaline phosphatase (PHO) secretory signal peptide (i.e., leader) located upstream of a multiple cloning site.

Many other yeast vectors could be used in place of pPIC9K, such as, pYES2, pYD1, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalpha, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, and PAO815, as one skilled in the art would readily appreciate, as long as the proposed expression construct provides appropriately located signals for transcription, translation, secretion (if desired), and the like, including an in-frame AUG as required.

In another embodiment, high-level expression of a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, may be achieved by cloning the heterologous polynucleotide of the invention into an expression vector such as, for example, pGAPZ or pGAPZalpha, and growing the yeast culture in the absence of methanol.

In addition to encompassing host cells containing the vector constructs discussed herein, the invention also encompasses primary, secondary, and immortalized host cells of vertebrate origin, particularly mammalian origin, that have been engineered to delete or replace endogenous genetic material (e.g., coding sequence), and/or to include genetic material (e.g., heterologous polynucleotide sequences) that is operably associated with polynucleotides of the invention, and which activates, alters, and/or amplifies endogenous polynucleotides. For example, techniques known in the art may be used to operably associate heterologous control regions (e.g., promoter and/or enhancer) and endogenous polynucleotide sequences via homologous recombination (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., *Proc. Natl. Acad. Sci. USA* 86:8932-8935 (1989); and Zijlstra et al., *Nature* 342:435-438 (1989), the disclosures of each of which are incorporated by reference in their entireties).

In addition, polypeptides of the invention can be chemically synthesized using techniques known in the art (e.g., see Creighton, 1983, *Proteins: Structures and Molecular Principles*, W.H. Freeman & Co., N.Y., and Hunkapiller et al., *Nature*, 310:105-111 (1984)). For example, a polypeptide corresponding to a fragment of a polypeptide can be synthesized by use of a peptide synthesizer. Furthermore, if desired, nonclassical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the polypeptide sequence. Non-classical amino acids include, but are not limited to, to the D-isomers of the common amino acids, 2,4-diaminobutyric acid, α -amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid, g-Abu, e-Ahx, 6-amino hexanoic acid, Aib, 2-amino isobutyric acid, 3-amino propionic acid, ornithine, norleucine, norvaline, hydroxyproline, sarcosine, citrulline, homocitrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, b-alanine, fluoro-amino acids, designer amino acids such as b-methyl amino acids, Ca-methyl amino acids, Na-methyl amino

acids, and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

The invention encompasses polypeptides of the present invention which are differentially modified during or after translation, e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited, to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, NaBH₄; acetylation, formylation, oxidation, reduction; metabolic synthesis in the presence of tunicamycin; etc.

Additional post-translational modifications encompassed by the invention include, for example, e.g., N-linked or O-linked carbohydrate chains, processing of N-terminal or C-terminal ends), attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of procaryotic host cell expression. The polypeptides may also be modified with a detectable label, such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the protein.

Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin; and examples of suitable radioactive material include iodine (¹²¹I, ¹²³I, ¹²⁵I, ¹³¹I), carbon (¹⁴C), sulfur (³⁵S), tritium (³H), indium (¹¹¹In, ¹¹²In, ^{113m}In, ^{115m}In), technetium (⁹⁹Tc, ^{99m}Tc), thallium (²⁰¹Tl), gallium (⁶⁸Ga, ⁶⁷Ga), palladium (¹⁰³Pd), molybdenum (⁹⁹Mo), xenon (¹³³Xe), fluorine (¹⁸F), ¹⁵³Sm, ¹⁷⁷Lu, ¹⁵⁹Gd, ¹⁴⁹Pm, ¹⁴⁰La, ¹⁷³Yb, ¹⁶⁶Ho, ⁹⁰Y, ⁴⁷Sc, ¹⁸⁶Re, ¹⁸⁸Re, ¹⁴²Pr, ¹⁰⁵Rh, and ⁹⁷Ru.

In specific embodiments, a polypeptide of the present invention or fragment or variant thereof is attached to macrocyclic chelators that associate with radiometal ions, including but not limited to, ¹⁷⁷Lu, ⁹⁰Y, ¹⁶⁶Ho, and ¹⁵³Sm, to polypeptides. In a preferred embodiment, the radiometal ion associated with the macrocyclic chelators is ¹¹¹In. In another preferred embodiment, the radiometal ion associated with the macrocyclic chelator is ⁹⁰Y. In specific embodiments, the macrocyclic chelator is 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA). In other specific embodiments, DOTA is attached to an antibody of the invention or fragment thereof via a linker molecule. Examples of linker molecules useful for conjugating DOTA to a polypeptide are commonly known in the art - see, for example, DeNardo et al., Clin Cancer Res. 4(10):2483-90 (1998); Peterson et al., Bioconjug. Chem. 10(4):553-7 (1999); and

Zimmerman et al, Nucl. Med. Biol. 26(8):943-50 (1999); which are hereby incorporated by reference in their entirety.

As mentioned, the proteins of the invention may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Polypeptides of the invention may be branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth. Enzymol. 182:626-646 (1990); Rattan et al., Ann. N.Y. Acad. Sci. 663:48-62 (1992)).

Also provided by the invention are chemically modified derivatives of the polypeptides of the invention which may provide additional advantages such as increased solubility, stability and circulating time of the polypeptide, or decreased immunogenicity (see U.S. Patent No. 4,179,337). The chemical moieties for derivitization may be selected from water soluble polymers such as polyethylene glycol, ethylene glycol/propylene glycol copolymers, carboxymethylcellulose, dextran, polyvinyl alcohol and the like. The polypeptides may be modified at random positions within the molecule, or at predetermined positions within the molecule and may include one, two, three or more attached chemical moieties.

The polymer may be of any molecular weight, and may be branched or unbranched. For polyethylene glycol, the preferred molecular weight is between about 1 kDa and about 100 kDa (the term "about" indicating that in preparations of polyethylene glycol, some molecules will weigh more, some less, than the stated molecular weight) for ease in handling and manufacturing. Other sizes may be used, depending on the desired therapeutic profile (e.g., the duration of sustained release desired, the effects, if any on biological activity, the ease in handling, the degree or lack of antigenicity and other known effects of the polyethylene glycol to a therapeutic protein

or analog). For example, the polyethylene glycol may have an average molecular weight of about 200, 500, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500, 5000, 5500, 6000, 6500, 7000, 7500, 8000, 8500, 9000, 9500, 10,000, 10,500, 11,000, 11,500, 12,000, 12,500, 13,000, 13,500, 14,000, 14,500, 15,000, 15,500, 16,000, 16,500, 17,000, 17,500, 18,000, 18,500, 19,000, 19,500, 20,000, 25,000, 30,000, 35,000, 40,000, 45,000, 50,000, 55,000, 60,000, 65,000, 70,000, 75,000, 80,000, 85,000, 90,000, 95,000, or 100,000 kDa.

As noted above, the polyethylene glycol may have a branched structure. Branched polyethylene glycols are described, for example, in U.S. Patent No. 5,643,575; Morpurgo *et al.*, *Appl. Biochem. Biotechnol.* 56:59-72 (1996); Vorobjev *et al.*, *Nucleosides Nucleotides* 18:2745-2750 (1999); and Caliceti *et al.*, *Bioconjug. Chem.* 10:638-646 (1999), the disclosures of each of which are incorporated herein by reference.

The polyethylene glycol molecules (or other chemical moieties) should be attached to the protein with consideration of effects on functional or antigenic domains of the protein. There are a number of attachment methods available to those skilled in the art, such as, for example, the method disclosed in EP 0 401 384 (coupling PEG to G-CSF), herein incorporated by reference; see also Malik *et al.*, *Exp. Hematol.* 20:1028-1035 (1992), reporting pegylation of GM-CSF using tresyl chloride. For example, polyethylene glycol may be covalently bound through amino acid residues via a reactive group, such as a free amino or carboxyl group. Reactive groups are those to which an activated polyethylene glycol molecule may be bound. The amino acid residues having a free amino group may include lysine residues and the N-terminal amino acid residues; those having a free carboxyl group may include aspartic acid residues glutamic acid residues and the C-terminal amino acid residue. Sulfhydryl groups may also be used as a reactive group for attaching the polyethylene glycol molecules. Preferred for therapeutic purposes is attachment at an amino group, such as attachment at the N-terminus or lysine group.

As suggested above, polyethylene glycol may be attached to proteins via linkage to any of a number of amino acid residues. For example, polyethylene glycol can be linked to proteins via covalent bonds to lysine, histidine, aspartic acid, glutamic acid, or cysteine residues. One or more reaction chemistries may be employed to attach polyethylene glycol to specific amino acid residues (e.g., lysine, histidine, aspartic acid, glutamic acid, or cysteine) of the protein or to more than one type of amino acid residue (e.g., lysine, histidine, aspartic acid, glutamic acid, cysteine and combinations thereof) of the protein.

One may specifically desire proteins chemically modified at the N-terminus. Using polyethylene glycol as an illustration of the present composition, one may select from a variety of polyethylene glycol molecules (by molecular weight, branching, etc.), the proportion of polyethylene glycol molecules to protein (polypeptide) molecules in the reaction mix, the type of pegylation reaction to be performed, and the method of obtaining the selected N-terminally pegylated protein. The method of obtaining the N-terminally pegylated preparation (i.e.,

separating this moiety from other monopegylated moieties if necessary) may be by purification of the N-terminally pegylated material from a population of pegylated protein molecules. Selective proteins chemically modified at the N-terminus modification may be accomplished by reductive alkylation which exploits differential reactivity of different types of primary amino groups (lysine
5 versus the N-terminal) available for derivatization in a particular protein. Under the appropriate reaction conditions, substantially selective derivatization of the protein at the N-terminus with a carbonyl group containing polymer is achieved.

As indicated above, pegylation of the proteins of the invention may be accomplished by any number of means. For example, polyethylene glycol may be attached to the protein either
10 directly or by an intervening linker. Linkerless systems for attaching polyethylene glycol to proteins are described in Delgado et al., Crit. Rev. Thera. Drug Carrier Sys. 9:249-304 (1992); Francis et al., Intern. J. of Hematol. 68:1-18 (1998); U.S. Patent No. 4,002,531; U.S. Patent No. 5,349,052; WO 95/06058; and WO 98/32466, the disclosures of each of which are incorporated herein by reference.

15 One system for attaching polyethylene glycol directly to amino acid residues of proteins without an intervening linker employs tresylated MPEG, which is produced by the modification of monmethoxy polyethylene glycol (MPEG) using tresylchloride ($\text{ClSO}_2\text{CH}_2\text{CF}_3$). Upon reaction of protein with tresylated MPEG, polyethylene glycol is directly attached to amine groups of the protein. Thus, the invention includes protein-polyethylene glycol conjugates produced by reacting
20 proteins of the invention with a polyethylene glycol molecule having a 2,2,2-trifluoroethane sulphonyl group.

Polyethylene glycol can also be attached to proteins using a number of different intervening linkers. For example, U.S. Patent No. 5,612,460, the entire disclosure of which is incorporated herein by reference, discloses urethane linkers for connecting polyethylene glycol to
25 proteins. Protein-polyethylene glycol conjugates wherein the polyethylene glycol is attached to the protein by a linker can also be produced by reaction of proteins with compounds such as MPEG-succinimidylsuccinate, MPEG activated with 1,1'-carbonyldiimidazole, MPEG-2,4,5-trichloropenylcarbonate, MPEG-p-nitrophenolcarbonate, and various MPEG-succinate derivatives. A number of additional polyethylene glycol derivatives and reaction chemistries for
30 attaching polyethylene glycol to proteins are described in International Publication No. WO 98/32466, the entire disclosure of which is incorporated herein by reference. Pegylated protein products produced using the reaction chemistries set out herein are included within the scope of the invention.

The number of polyethylene glycol moieties attached to each protein of the invention (i.e.,
35 the degree of substitution) may also vary. For example, the pegylated proteins of the invention may be linked, on average, to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, 17, 20, or more polyethylene glycol molecules. Similarly, the average degree of substitution within ranges such as 1-3, 2-4, 3-5,

4-6, 5-7, 6-8, 7-9, 8-10, 9-11, 10-12, 11-13, 12-14, 13-15, 14-16, 15-17, 16-18, 17-19, or 18-20 polyethylene glycol moieties per protein molecule. Methods for determining the degree of substitution are discussed, for example, in Delgado et al., Crit. Rev. Thera. Drug Carrier Sys. 9:249-304 (1992).

5 The polypeptides of the invention can be recovered and purified from chemical synthesis and recombinant cell cultures by standard methods which include, but are not limited to, ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most
10 preferably, high performance liquid chromatography ("HPLC") is employed for purification. Well known techniques for refolding protein may be employed to regenerate active conformation when the polypeptide is denatured during isolation and/or purification.

 The polypeptides of the invention may be in monomers or multimers (i.e., dimers, trimers, tetramers and higher multimers). Accordingly, the present invention relates to monomers and
15 multimers of the polypeptides of the invention, their preparation, and compositions (preferably, Therapeutics) containing them. In specific embodiments, the polypeptides of the invention are monomers, dimers, trimers or tetramers. In additional embodiments, the multimers of the invention are at least dimers, at least trimers, or at least tetramers.

 Multimers encompassed by the invention may be homomers or heteromers. As used
20 herein, the term homomer refers to a multimer containing only polypeptides corresponding to a protein of the invention (e.g., the amino acid sequence of SEQ ID NO:Y, an amino acid sequence encoded by SEQ ID NO:X or the complement of SEQ ID NO:X, the amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or an amino acid sequence encoded by cDNA contained in ATCC Deposit No:Z (including fragments, variants,
25 splice variants, and fusion proteins, corresponding to these as described herein)). These homomers may contain polypeptides having identical or different amino acid sequences. In a specific embodiment, a homomer of the invention is a multimer containing only polypeptides having an identical amino acid sequence. In another specific embodiment, a homomer of the invention is a multimer containing polypeptides having different amino acid sequences. In specific
30 embodiments, the multimer of the invention is a homodimer (e.g., containing two polypeptides having identical or different amino acid sequences) or a homotrimer (e.g., containing three polypeptides having identical and/or different amino acid sequences). In additional embodiments, the homomeric multimer of the invention is at least a homodimer, at least a homotrimer, or at least a homotetramer.

35 As used herein, the term heteromer refers to a multimer containing one or more heterologous polypeptides (i.e., polypeptides of different proteins) in addition to the polypeptides of the invention. In a specific embodiment, the multimer of the invention is a heterodimer, a

heterotrimer, or a heterotetramer. In additional embodiments, the heteromeric multimer of the invention is at least a heterodimer, at least a heterotrimer, or at least a heterotetramer.

Multimers of the invention may be the result of hydrophobic, hydrophilic, ionic and/or covalent associations and/or may be indirectly linked by, for example, liposome formation. Thus, in one embodiment, multimers of the invention, such as, for example, homodimers or homotrimers, are formed when polypeptides of the invention contact one another in solution. In another embodiment, heteromultimers of the invention, such as, for example, heterotrimers or heterotetramers, are formed when polypeptides of the invention contact antibodies to the polypeptides of the invention (including antibodies to the heterologous polypeptide sequence in a fusion protein of the invention) in solution. In other embodiments, multimers of the invention are formed by covalent associations with and/or between the polypeptides of the invention. Such covalent associations may involve one or more amino acid residues contained in the polypeptide sequence (e.g., that recited in SEQ ID NO:Y, encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or encoded by the cDNA contained in ATCC Deposit No:Z). In one instance, the covalent associations are cross-linking between cysteine residues located within the polypeptide sequences which interact in the native (i.e., naturally occurring) polypeptide. In another instance, the covalent associations are the consequence of chemical or recombinant manipulation. Alternatively, such covalent associations may involve one or more amino acid residues contained in the heterologous polypeptide sequence in a fusion protein. In one example, covalent associations are between the heterologous sequence contained in a fusion protein of the invention (see, e.g., US Patent Number 5,478,925). In a specific example, the covalent associations are between the heterologous sequence contained in a Fc fusion protein of the invention (as described herein). In another specific example, covalent associations of fusion proteins of the invention are between heterologous polypeptide sequence from another protein that is capable of forming covalently associated multimers, such as for example, osteoprotegerin (see, e.g., International Publication NO: WO 98/49305, the contents of which are herein incorporated by reference in its entirety). In another embodiment, two or more polypeptides of the invention are joined through peptide linkers. Examples include those peptide linkers described in U.S. Pat. No. 5,073,627 (hereby incorporated by reference). Proteins comprising multiple polypeptides of the invention separated by peptide linkers may be produced using conventional recombinant DNA technology.

Another method for preparing multimer polypeptides of the invention involves use of polypeptides of the invention fused to a leucine zipper or isoleucine zipper polypeptide sequence. Leucine zipper and isoleucine zipper domains are polypeptides that promote multimerization of the proteins in which they are found. Leucine zippers were originally identified in several DNA-binding proteins (Landschulz et al., Science 240:1759, (1988)), and have since been found in a variety of different proteins. Among the known leucine zippers are naturally occurring peptides

and derivatives thereof that dimerize or trimerize. Examples of leucine zipper domains suitable for producing soluble multimeric proteins of the invention are those described in PCT application WO 94/10308, hereby incorporated by reference. Recombinant fusion proteins comprising a polypeptide of the invention fused to a polypeptide sequence that dimerizes or trimerizes in solution are expressed in suitable host cells, and the resulting soluble multimeric fusion protein is recovered from the culture supernatant using techniques known in the art.

Trimeric polypeptides of the invention may offer the advantage of enhanced biological activity. Preferred leucine zipper moieties and isoleucine moieties are those that preferentially form trimers. One example is a leucine zipper derived from lung surfactant protein D (SPD), as described in Hoppe et al. (FEBS Letters 344:191, (1994)) and in U.S. patent application Ser. No. 08/446,922, hereby incorporated by reference. Other peptides derived from naturally occurring trimeric proteins may be employed in preparing trimeric polypeptides of the invention.

In another example, proteins of the invention are associated by interactions between Flag® polypeptide sequence contained in fusion proteins of the invention containing Flag® polypeptide sequence. In a further embodiment, proteins of the invention are associated by interactions between heterologous polypeptide sequence contained in Flag® fusion proteins of the invention and anti-Flag® antibody.

The multimers of the invention may be generated using chemical techniques known in the art. For example, polypeptides desired to be contained in the multimers of the invention may be chemically cross-linked using linker molecules and linker molecule length optimization techniques known in the art (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, multimers of the invention may be generated using techniques known in the art to form one or more inter-molecule cross-links between the cysteine residues located within the sequence of the polypeptides desired to be contained in the multimer (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Further, polypeptides of the invention may be routinely modified by the addition of cysteine or biotin to the C-terminus or N-terminus of the polypeptide and techniques known in the art may be applied to generate multimers containing one or more of these modified polypeptides (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, techniques known in the art may be applied to generate liposomes containing the polypeptide components desired to be contained in the multimer of the invention (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

Alternatively, multimers of the invention may be generated using genetic engineering techniques known in the art. In one embodiment, polypeptides contained in multimers of the invention are produced recombinantly using fusion protein technology described herein or otherwise known in the art (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In a specific embodiment, polynucleotides coding for a homodimer of

the invention are generated by ligating a polynucleotide sequence encoding a polypeptide of the invention to a sequence encoding a linker polypeptide and then further to a synthetic polynucleotide encoding the translated product of the polypeptide in the reverse orientation from the original C-terminus to the N-terminus (lacking the leader sequence) (see, e.g., US Patent
5 Number 5,478,925, which is herein incorporated by reference in its entirety). In another embodiment, recombinant techniques described herein or otherwise known in the art are applied to generate recombinant polypeptides of the invention which contain a transmembrane domain (or hydrophobic or signal peptide) and which can be incorporated by membrane reconstitution techniques into liposomes (see, e.g., US Patent Number 5,478,925, which is herein incorporated by
10 reference in its entirety).

Antibodies

Further polypeptides of the invention relate to antibodies and T-cell antigen receptors (TCR) which immunospecifically bind a polypeptide, polypeptide fragment, or variant of the invention (e.g., a polypeptide or fragment or variant of the amino acid sequence of SEQ ID NO:Y or a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z, and/or an epitope, of the present invention) as determined by immunoassays well known in the art for assaying specific antibody-antigen binding. Antibodies of the invention include, but are not limited to, polyclonal, monoclonal, multispecific, human, humanized or chimeric antibodies, single chain antibodies, Fab
15 fragments, F(ab') fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id antibodies to antibodies of the invention), intracellularly-made antibodies (i.e., intrabodies), and epitope-binding fragments of any of the above. The term "antibody," as used herein, refers to immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, i.e., molecules that contain an antigen binding site that
20 immunospecifically binds an antigen. The immunoglobulin molecules of the invention can be of any type (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass of immunoglobulin molecule. In preferred embodiments, the immunoglobulin molecules of the invention are IgG1. In other preferred embodiments, the immunoglobulin molecules of the invention are IgG4.

30 Most preferably the antibodies are human antigen-binding antibody fragments of the present invention and include, but are not limited to, Fab, Fab' and F(ab')₂, Fd, single-chain Fvs (scFv), single-chain antibodies, disulfide-linked Fvs (sdFv) and fragments comprising either a VL or VH domain. Antigen-binding antibody fragments, including single-chain antibodies, may comprise the variable region(s) alone or in combination with the entirety or a portion of the
35 following: hinge region, CH1, CH2, and CH3 domains. Also included in the invention are antigen-binding fragments also comprising any combination of variable region(s) with a hinge region, CH1, CH2, and CH3 domains. The antibodies of the invention may be from any animal

origin including birds and mammals. Preferably, the antibodies are human, murine (e.g., mouse and rat), donkey, sheep rabbit, goat, guinea pig, camel, horse, or chicken. As used herein, "human" antibodies include antibodies having the amino acid sequence of a human immunoglobulin and include antibodies isolated from human immunoglobulin libraries or from animals transgenic for one or more human immunoglobulin and that do not express endogenous immunoglobulins, as described infra and, for example in, U.S. Patent No. 5,939,598 by Kucherlapati et al.

The antibodies of the present invention may be monospecific, bispecific, trispecific or of greater multispecificity. Multispecific antibodies may be specific for different epitopes of a polypeptide of the present invention or may be specific for both a polypeptide of the present invention as well as for a heterologous epitope, such as a heterologous polypeptide or solid support material. See, e.g., PCT publications WO 93/17715; WO 92/08802; WO 91/00360; WO 92/05793; Tutt, et al., J. Immunol. 147:60-69 (1991); U.S. Patent Nos. 4,474,893; 4,714,681; 4,925,648; 5,573,920; 5,601,819; Kostelny et al., J. Immunol. 148:1547-1553 (1992).

Antibodies of the present invention may be described or specified in terms of the epitope(s) or portion(s) of a polypeptide of the present invention which they recognize or specifically bind. The epitope(s) or polypeptide portion(s) may be specified as described herein, e.g., by N-terminal and C-terminal positions, or by size in contiguous amino acid residues, or listed in the Tables and Figures. Preferred epitopes of the invention include the predicted epitopes shown in column 7 of Table 1B.1, as well as polynucleotides that encode these epitopes. Antibodies which specifically bind any epitope or polypeptide of the present invention may also be excluded. Therefore, the present invention includes antibodies that specifically bind polypeptides of the present invention, and allows for the exclusion of the same.

Antibodies of the present invention may also be described or specified in terms of their cross-reactivity. Antibodies that do not bind any other analog, ortholog, or homolog of a polypeptide of the present invention are included. Antibodies that bind polypeptides with at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, and at least 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In specific embodiments, antibodies of the present invention cross-react with murine, rat and/or rabbit homologs of human proteins and the corresponding epitopes thereof. Antibodies that do not bind polypeptides with less than 95%, less than 90%, less than 85%, less than 80%, less than 75%, less than 70%, less than 65%, less than 60%, less than 55%, and less than 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In a specific embodiment, the above-described cross-reactivity is with respect to any single specific antigenic or immunogenic polypeptide, or combination(s) of 2, 3, 4, 5, or more of the specific antigenic and/or immunogenic polypeptides disclosed herein. Further included in the present invention are antibodies which bind

polypeptides encoded by polynucleotides which hybridize to a polynucleotide of the present invention under stringent hybridization conditions (as described herein). Antibodies of the present invention may also be described or specified in terms of their binding affinity to a polypeptide of the invention. Preferred binding affinities include those with a dissociation constant or K_d less than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, or 10^{-15} M.

The invention also provides antibodies that competitively inhibit binding of an antibody to an epitope of the invention as determined by any method known in the art for determining competitive binding, for example, the immunoassays described herein. In preferred embodiments, the antibody competitively inhibits binding to the epitope by at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50%.

Antibodies of the present invention may act as agonists or antagonists of the polypeptides of the present invention. For example, the present invention includes antibodies which disrupt the receptor/ligand interactions with the polypeptides of the invention either partially or fully. Preferably, antibodies of the present invention bind an antigenic epitope disclosed herein, or a portion thereof. The invention features both receptor-specific antibodies and ligand-specific antibodies. The invention also features receptor-specific antibodies which do not prevent ligand binding but prevent receptor activation. Receptor activation (i.e., signaling) may be determined by techniques described herein or otherwise known in the art. For example, receptor activation can be determined by detecting the phosphorylation (e.g., tyrosine or serine/threonine) of the receptor or its substrate by immunoprecipitation followed by western blot analysis (for example, as described *supra*). In specific embodiments, antibodies are provided that inhibit ligand activity or receptor activity by at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50% of the activity in absence of the antibody.

The invention also features receptor-specific antibodies which both prevent ligand binding and receptor activation as well as antibodies that recognize the receptor-ligand complex, and, preferably, do not specifically recognize the unbound receptor or the unbound ligand. Likewise, included in the invention are neutralizing antibodies which bind the ligand and prevent binding of the ligand to the receptor, as well as antibodies which bind the ligand, thereby preventing receptor activation, but do not prevent the ligand from binding the receptor. Further included in the invention are antibodies which activate the receptor. These antibodies may act as receptor agonists, i.e., potentiate or activate either all or a subset of the biological activities of the ligand-mediated receptor activation, for example, by inducing dimerization of the receptor. The antibodies may be specified as agonists, antagonists or inverse agonists for biological activities comprising the specific biological activities of the peptides of the invention disclosed herein. The

above antibody agonists can be made using methods known in the art. See, e.g., PCT publication WO 96/40281; U.S. Patent No. 5,811,097; Deng et al., Blood 92(6):1981-1988 (1998); Chen et al., Cancer Res. 58(16):3668-3678 (1998); Harrop et al., J. Immunol. 161(4):1786-1794 (1998); Zhu et al., Cancer Res. 58(15):3209-3214 (1998); Yoon et al., J. Immunol. 160(7):3170-3179 (1998);
5 Prat et al., J. Cell. Sci. 111(Pt2):237-247 (1998); Pitard et al., J. Immunol. Methods 205(2):177-190 (1997); Liautard et al., Cytokine 9(4):233-241 (1997); Carlson et al., J. Biol. Chem. 272(17):11295-11301 (1997); Taryman et al., Neuron 14(4):755-762 (1995); Muller et al., Structure 6(9):1153-1167 (1998); Bartunek et al., Cytokine 8(1):14-20 (1996) (which are all incorporated by reference herein in their entireties).

10 Antibodies of the present invention may be used, for example, to purify, detect, and target the polypeptides of the present invention, including both *in vitro* and *in vivo* diagnostic and therapeutic methods. For example, the antibodies have utility in immunoassays for qualitatively and quantitatively measuring levels of the polypeptides of the present invention in biological samples. See, e.g., Harlow et al., Antibodies: A Laboratory Manual, (Cold Spring Harbor
15 Laboratory Press, 2nd ed. 1988); incorporated by reference herein in its entirety.

As discussed in more detail below, the antibodies of the present invention may be used either alone or in combination with other compositions. The antibodies may further be recombinantly fused to a heterologous polypeptide at the N- or C-terminus or chemically conjugated (including covalent and non-covalent conjugations) to polypeptides or other
20 compositions. For example, antibodies of the present invention may be recombinantly fused or conjugated to molecules useful as labels in detection assays and effector molecules such as heterologous polypeptides, drugs, radionuclides, or toxins. See, e.g., PCT publications WO 92/08495; WO 91/14438; WO 89/12624; U.S. Patent No. 5,314,995; and EP 396,387; the disclosures of which are incorporated herein by reference in their entireties.

25 The antibodies of the invention include derivatives that are modified, i.e., by the covalent attachment of any type of molecule to the antibody such that covalent attachment does not prevent the antibody from generating an anti-idiotypic response. For example, but not by way of limitation, the antibody derivatives include antibodies that have been modified, e.g., by glycosylation, acetylation, pegylation, phosphorylation, amidation, derivatization by known
30 protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein, etc. Any of numerous chemical modifications may be carried out by known techniques, including, but not limited to specific chemical cleavage, acetylation, formylation, metabolic synthesis of tunicamycin, etc. Additionally, the derivative may contain one or more non-classical amino acids.

The antibodies of the present invention may be generated by any suitable method known
35 in the art. Polyclonal antibodies to an antigen-of-interest can be produced by various procedures well known in the art. For example, a polypeptide of the invention can be administered to various host animals including, but not limited to, rabbits, mice, rats, etc. to induce the production of sera

containing polyclonal antibodies specific for the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, 5 keyhole limpet hemocyanins, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and corynebacterium parvum. Such adjuvants are also well known in the art.

Monoclonal antibodies can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques 10 including those known in the art and taught, for example, in Harlow et al., *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, et al., in: *Monoclonal Antibodies and T-Cell Hybridomas* 563-681 (Elsevier, N.Y., 1981) (said references incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is 15 not limited to antibodies produced through hybridoma technology. The term "monoclonal antibody" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.

Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art and are discussed in detail in the Examples. In a non- 20 limiting example, mice can be immunized with a polypeptide of the invention or a cell expressing such peptide. Once an immune response is detected, e.g., antibodies specific for the antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells, for example cells from cell line SP20 available from the ATCC. Hybridomas are selected and cloned by 25 limited dilution. The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding a polypeptide of the invention. Ascites fluid, which generally contains high levels of antibodies, can be generated by immunizing mice with positive hybridoma clones.

Accordingly, the present invention provides methods of generating monoclonal antibodies 30 as well as antibodies produced by the method comprising culturing a hybridoma cell secreting an antibody of the invention wherein, preferably, the hybridoma is generated by fusing splenocytes isolated from a mouse immunized with an antigen of the invention with myeloma cells and then screening the hybridomas resulting from the fusion for hybridoma clones that secrete an antibody able to bind a polypeptide of the invention.

35 Another well known method for producing both polyclonal and monoclonal human B cell lines is transformation using Epstein Barr Virus (EBV). Protocols for generating EBV-transformed B cell lines are commonly known in the art, such as, for example, the protocol

outlined in Chapter 7.22 of Current Protocols in Immunology, Coligan et al., Eds., 1994, John Wiley & Sons, NY, which is hereby incorporated in its entirety by reference. The source of B cells for transformation is commonly human peripheral blood, but B cells for transformation may also be derived from other sources including, but not limited to, lymph nodes, tonsil, spleen, tumor
5 tissue, and infected tissues. Tissues are generally made into single cell suspensions prior to EBV transformation. Additionally, steps may be taken to either physically remove or inactivate T cells (e.g., by treatment with cyclosporin A) in B cell-containing samples, because T cells from individuals seropositive for anti-EBV antibodies can suppress B cell immortalization by EBV.

In general, the sample containing human B cells is inoculated with EBV, and cultured for
10 3-4 weeks. A typical source of EBV is the culture supernatant of the B95-8 cell line (ATCC #VR-1492). Physical signs of EBV transformation can generally be seen towards the end of the 3-4 week culture period. By phase-contrast microscopy, transformed cells may appear large, clear, hairy and tend to aggregate in tight clusters of cells. Initially, EBV lines are generally polyclonal. However, over prolonged periods of cell cultures, EBV lines may become monoclonal or
15 polyclonal as a result of the selective outgrowth of particular B cell clones. Alternatively, polyclonal EBV transformed lines may be subcloned (e.g., by limiting dilution culture) or fused with a suitable fusion partner and plated at limiting dilution to obtain monoclonal B cell lines. Suitable fusion partners for EBV transformed cell lines include mouse myeloma cell lines (e.g., SP2/0, X63-Ag8.653), heteromyeloma cell lines (human x mouse; e.g., SPAM-8, SBC-H20, and
20 CB-F7), and human cell lines (e.g., GM 1500, SKO-007, RPMI 8226, and KR-4). Thus, the present invention also provides a method of generating polyclonal or monoclonal human antibodies against polypeptides of the invention or fragments thereof, comprising EBV-transformation of human B cells.

Antibody fragments which recognize specific epitopes may be generated by known
25 techniques. For example, Fab and F(ab')₂ fragments of the invention may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')₂ fragments). F(ab')₂ fragments contain the variable region, the light chain constant region and the CH1 domain of the heavy chain.

For example, the antibodies of the present invention can also be generated using various
30 phage display methods known in the art. In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In a particular embodiment, such phage can be utilized to display antigen binding domains expressed from a repertoire or combinatorial antibody library (e.g., human or murine). Phage expressing an antigen binding domain that binds the antigen of interest can be selected or
35 identified with antigen, e.g., using labeled antigen or antigen bound or captured to a solid surface or bead. Phage used in these methods are typically filamentous phage including fd and M13 binding domains expressed from phage with Fab, Fv or disulfide stabilized Fv antibody domains

recombinantly fused to either the phage gene III or gene VIII protein. Examples of phage display methods that can be used to make the antibodies of the present invention include those disclosed in Brinkman et al., J. Immunol. Methods 182:41-50 (1995); Ames et al., J. Immunol. Methods 184:177-186 (1995); Kettleborough et al., Eur. J. Immunol. 24:952-958 (1994); Persic et al., Gene
5 187 9-18 (1997); Burton et al., Advances in Immunology 57:191-280 (1994); PCT application No. PCT/GB91/01134; PCT publications WO 90/02809; WO 91/10737; WO 92/01047; WO 92/18619; WO 93/11236; WO 95/15982; WO 95/20401; and U.S. Patent Nos. 5,698,426; 5,223,409; 5,403,484; 5,580,717; 5,427,908; 5,750,753; 5,821,047; 5,571,698; 5,427,908; 5,516,637; 5,780,225; 5,658,727; 5,733,743 and 5,969,108; each of which is incorporated herein
10 by reference in its entirety.

As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies, including human antibodies, or any other desired antigen binding fragment, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, e.g., as described in detail below.
15 For example, techniques to recombinantly produce Fab, Fab' and F(ab')₂ fragments can also be employed using methods known in the art such as those disclosed in PCT publication WO 92/22324; Mullinax et al., BioTechniques 12(6):864-869 (1992); and Sawai et al., AJRI 34:26-34 (1995); and Better et al., Science 240:1041-1043 (1988) (said references incorporated by reference in their entireties).

20 Examples of techniques which can be used to produce single-chain Fvs and antibodies include those described in U.S. Patents 4,946,778 and 5,258,498; Huston et al., Methods in Enzymology 203:46-88 (1991); Shu et al., PNAS 90:7995-7999 (1993); and Skerra et al., Science 240:1038-1040 (1988). For some uses, including *in vivo* use of antibodies in humans and *in vitro* detection assays, it may be preferable to use chimeric, humanized, or human antibodies. A
25 chimeric antibody is a molecule in which different portions of the antibody are derived from different animal species, such as antibodies having a variable region derived from a murine monoclonal antibody and a human immunoglobulin constant region. Methods for producing chimeric antibodies are known in the art. See e.g., Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Gillies et al., (1989) J. Immunol. Methods 125:191-202; U.S. Patent
30 Nos. 5,807,715; 4,816,567; and 4,816,397, which are incorporated herein by reference in their entirety. Humanized antibodies are antibody molecules from non-human species antibody that binds the desired antigen having one or more complementarity determining regions (CDRs) from the non-human species and a framework regions from a human immunoglobulin molecule. Often, framework residues in the human framework regions will be substituted with the corresponding
35 residue from the CDR donor antibody to alter, preferably improve, antigen binding. These framework substitutions are identified by methods well known in the art, e.g., by modeling of the interactions of the CDR and framework residues to identify framework residues important for

antigen binding and sequence comparison to identify unusual framework residues at particular positions. (See, e.g., Queen et al., U.S. Patent No. 5,585,089; Riechmann et al., Nature 332:323 (1988), which are incorporated herein by reference in their entireties.) Antibodies can be humanized using a variety of techniques known in the art including, for example, CDR-grafting
5 (EP 239,400; PCT publication WO 91/09967; U.S. Patent Nos. 5,225,539; 5,530,101; and 5,585,089), veneering or resurfacing (EP 592,106; EP 519,596; Padlan, Molecular Immunology 28(4/5):489-498 (1991); Studnicka et al., Protein Engineering 7(6):805-814 (1994); Roguska. et al., PNAS 91:969-973 (1994)), and chain shuffling (U.S. Patent No. 5,565,332).

Completely human antibodies are particularly desirable for therapeutic treatment of human
10 patients. Human antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody libraries derived from human immunoglobulin sequences. See also, U.S. Patent Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645, WO 98/50433, WO 98/24893, WO 98/16654, WO 96/34096, WO 96/33735, and WO 91/10741; each of which is incorporated herein by reference in its entirety.

Human antibodies can also be produced using transgenic mice which are incapable of
15 expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. For example, the human heavy and light chain immunoglobulin gene complexes may be introduced randomly or by homologous recombination into mouse embryonic stem cells. Alternatively, the human variable region, constant region, and diversity region may be
20 introduced into mouse embryonic stem cells in addition to the human heavy and light chain genes. The mouse heavy and light chain immunoglobulin genes may be rendered non-functional separately or simultaneously with the introduction of human immunoglobulin loci by homologous recombination. In particular, homozygous deletion of the JH region prevents endogenous antibody
25 production. The modified embryonic stem cells are expanded and microinjected into blastocysts to produce chimeric mice. The chimeric mice are then bred to produce homozygous offspring which express human antibodies. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against the antigen can be obtained from the immunized, transgenic mice using
30 conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA, IgM and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, Int. Rev. Immunol. 13:65-93 (1995). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies
35 and protocols for producing such antibodies, see, e.g., PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; European Patent No. 0 598 877; U.S. Patent Nos. 5,413,923; 5,625,126; 5,633,425; 5,569,825; 5,661,016; 5,545,806; 5,814,318; 5,885,793;

5,916,771; 5,939,598; 6,075,181; and 6,114,598, which are incorporated by reference herein in their entirety. In addition, companies such as Abgenix, Inc. (Freemont, CA) and Genpharm (San Jose, CA) can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

5 Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a mouse antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., *Bio/technology* 12:899-903 (1988)).

Further, antibodies to the polypeptides of the invention can, in turn, be utilized to generate anti-idiotypic antibodies that "mimic" polypeptides of the invention using techniques well known to those skilled in the art. (See, e.g., Greenspan & Bona, *FASEB J.* 7(5):437-444; (1989) and Nissinoff, J. *Immunol.* 147(8):2429-2438 (1991)). For example, antibodies which bind to and competitively inhibit polypeptide multimerization and/or binding of a polypeptide of the invention to a ligand can be used to generate anti-idiotypes that "mimic" the polypeptide multimerization and/or binding domain and, as a consequence, bind to and neutralize polypeptide and/or its ligand. Such neutralizing anti-idiotypes or Fab fragments of such anti-idiotypes can be used in therapeutic regimens to neutralize polypeptide ligand(s)/receptor(s). For example, such anti-idiotypic antibodies can be used to bind a polypeptide of the invention and/or to bind its ligand(s)/receptor(s), and thereby block its biological activity. Alternatively, antibodies which bind to and enhance polypeptide multimerization and/or binding, and/or receptor/ligand multimerization, binding and/or signaling can be used to generate anti-idiotypes that function as agonists of a polypeptide of the invention and/or its ligand/receptor. Such agonistic anti-idiotypes or Fab fragments of such anti-idiotypes can be used in therapeutic regimens as agonists of the polypeptides of the invention or its ligand(s)/receptor(s). For example, such anti-idiotypic antibodies can be used to bind a polypeptide of the invention and/or to bind its ligand(s)/receptor(s), and thereby promote or enhance its biological activity.

Intrabodies of the invention can be produced using methods known in the art, such as those disclosed and reviewed in Chen et al., *Hum. Gene Ther.* 5:595-601 (1994); Marasco, W.A., *Gene Ther.* 4:11-15 (1997); Rondon and Marasco, *Annu. Rev. Microbiol.* 51:257-283 (1997); Proba et al., *J. Mol. Biol.* 275:245-253 (1998); Cohen et al., *Oncogene* 17:2445-2456 (1998); Ohage and Steipe, *J. Mol. Biol.* 291:1119-1128 (1999); Ohage et al., *J. Mol. Biol.* 291:1129-1134 (1999); Wirtz and Steipe, *Protein Sci.* 8:2245-2250 (1999); Zhu et al., *J. Immunol. Methods* 231:207-222 (1999); and references cited therein.

35 *Polynucleotides Encoding Antibodies*

The invention further provides polynucleotides comprising a nucleotide sequence encoding an antibody of the invention and fragments thereof. The invention also encompasses

polynucleotides that hybridize under stringent or alternatively, under lower stringency hybridization conditions, e.g., as defined *supra*, to polynucleotides that encode an antibody, preferably, that specifically binds to a polypeptide of the invention, preferably, an antibody that binds to a polypeptide having the amino acid sequence of SEQ ID NO:Y, to a polypeptide encoded by a portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or to a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z.

The polynucleotides may be obtained, and the nucleotide sequence of the polynucleotides determined, by any method known in the art. For example, if the nucleotide sequence of the antibody is known, a polynucleotide encoding the antibody may be assembled from chemically synthesized oligonucleotides (e.g., as described in Kutmeier et al., *BioTechniques* 17:242 (1994)), which, briefly, involves the synthesis of overlapping oligonucleotides containing portions of the sequence encoding the antibody, annealing and ligating of those oligonucleotides, and then amplification of the ligated oligonucleotides by PCR.

Alternatively, a polynucleotide encoding an antibody may be generated from nucleic acid from a suitable source. If a clone containing a nucleic acid encoding a particular antibody is not available, but the sequence of the antibody molecule is known, a nucleic acid encoding the immunoglobulin may be chemically synthesized or obtained from a suitable source (e.g., an antibody cDNA library, or a cDNA library generated from, or nucleic acid, preferably poly A+ RNA, isolated from, any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody of the invention) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence or by cloning using an oligonucleotide probe specific for the particular gene sequence to identify, e.g., a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR may then be cloned into replicable cloning vectors using any method well known in the art.

Once the nucleotide sequence and corresponding amino acid sequence of the antibody is determined, the nucleotide sequence of the antibody may be manipulated using methods well known in the art for the manipulation of nucleotide sequences, e.g., recombinant DNA techniques, site directed mutagenesis, PCR, etc. (see, for example, the techniques described in Sambrook et al., 1990, *Molecular Cloning, A Laboratory Manual*, 2d Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY and Ausubel et al., eds., 1998, *Current Protocols in Molecular Biology*, John Wiley & Sons, NY, which are both incorporated by reference herein in their entireties), to generate antibodies having a different amino acid sequence, for example to create amino acid substitutions, deletions, and/or insertions.

In a specific embodiment, the amino acid sequence of the heavy and/or light chain variable domains may be inspected to identify the sequences of the complementarity determining regions (CDRs) by methods that are well known in the art, e.g., by comparison to known amino acid sequences of other heavy and light chain variable regions to determine the regions of

sequence hypervariability. Using routine recombinant DNA techniques, one or more of the CDRs may be inserted within framework regions, e.g., into human framework regions to humanize a non-human antibody, as described *supra*. The framework regions may be naturally occurring or consensus framework regions, and preferably human framework regions (see, e.g., Chothia et al., J. Mol. Biol. 278: 457-479 (1998) for a listing of human framework regions). Preferably, the polynucleotide generated by the combination of the framework regions and CDRs encodes an antibody that specifically binds a polypeptide of the invention. Preferably, as discussed *supra*, one or more amino acid substitutions may be made within the framework regions, and, preferably, the amino acid substitutions improve binding of the antibody to its antigen. Additionally, such methods may be used to make amino acid substitutions or deletions of one or more variable region cysteine residues participating in an intrachain disulfide bond to generate antibody molecules lacking one or more intrachain disulfide bonds. Other alterations to the polynucleotide are encompassed by the present invention and within the skill of the art.

In addition, techniques developed for the production of "chimeric antibodies" (Morrison et al., Proc. Natl. Acad. Sci. 81:851-855 (1984); Neuberger et al., Nature 312:604-608 (1984); Takeda et al., Nature 314:452-454 (1985)) by splicing genes from a mouse antibody molecule of appropriate antigen specificity together with genes from a human antibody molecule of appropriate biological activity can be used. As described *supra*, a chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region, e.g., humanized antibodies.

Alternatively, techniques described for the production of single chain antibodies (U.S. Patent No. 4,946,778; Bird, Science 242:423-42 (1988); Huston et al., Proc. Natl. Acad. Sci. USA 85:5879-5883 (1988); and Ward et al., Nature 334:544-54 (1989)) can be adapted to produce single chain antibodies. Single chain antibodies are formed by linking the heavy and light chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide. Techniques for the assembly of functional Fv fragments in E. coli may also be used (Skerra et al., Science 242:1038-1041 (1988)).

Methods of Producing Antibodies

The antibodies of the invention can be produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques. Methods of producing antibodies include, but are not limited to, hybridoma technology, EBV transformation, and other methods discussed herein as well as through the use of recombinant DNA technology, as discussed below.

Recombinant expression of an antibody of the invention, or fragment, derivative or analog thereof, (e.g., a heavy or light chain of an antibody of the invention or a single chain antibody of

the invention), requires construction of an expression vector containing a polynucleotide that encodes the antibody. Once a polynucleotide encoding an antibody molecule or a heavy or light chain of an antibody, or portion thereof (preferably containing the heavy or light chain variable domain), of the invention has been obtained, the vector for the production of the antibody molecule may be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing a protein by expressing a polynucleotide containing an antibody encoding nucleotide sequence are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. The invention, thus, provides replicable vectors comprising a nucleotide sequence encoding an antibody molecule of the invention, or a heavy or light chain thereof, or a heavy or light chain variable domain, operably linked to a promoter. Such vectors may include the nucleotide sequence encoding the constant region of the antibody molecule (see, e.g., PCT Publication WO 86/05807; PCT Publication WO 89/01036; and U.S. Patent No. 5,122,464) and the variable domain of the antibody may be cloned into such a vector for expression of the entire heavy or light chain.

The expression vector is transferred to a host cell by conventional techniques and the transfected cells are then cultured by conventional techniques to produce an antibody of the invention. Thus, the invention includes host cells containing a polynucleotide encoding an antibody of the invention, or a heavy or light chain thereof, or a single chain antibody of the invention, operably linked to a heterologous promoter. In preferred embodiments for the expression of double-chained antibodies, vectors encoding both the heavy and light chains may be co-expressed in the host cell for expression of the entire immunoglobulin molecule, as detailed below.

A variety of host-expression vector systems may be utilized to express the antibody molecules of the invention. Such host-expression systems represent vehicles by which the coding sequences of interest may be produced and subsequently purified, but also represent cells which may, when transformed or transfected with the appropriate nucleotide coding sequences, express an antibody molecule of the invention *in situ*. These include but are not limited to microorganisms such as bacteria (e.g., *E. coli*, *B. subtilis*) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing antibody coding sequences; yeast (e.g., *Saccharomyces*, *Pichia*) transformed with recombinant yeast expression vectors containing antibody coding sequences; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing antibody coding sequences; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression

vectors (e.g., Ti plasmid) containing antibody coding sequences; or mammalian cell systems (e.g., COS, CHO, BHK, 293, 3T3 cells) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter).

5 Preferably, bacterial cells such as *Escherichia coli*, and more preferably, eukaryotic cells, especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant antibody molecule. For example, mammalian cells such as Chinese hamster ovary cells (CHO), in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for antibodies

10 (Foecking et al., *Gene* 45:101 (1986); Cockett et al., *Bio/Technology* 8:2 (1990)).

In bacterial systems, a number of expression vectors may be advantageously selected depending upon the use intended for the antibody molecule being expressed. For example, when a large quantity of such a protein is to be produced, for the generation of pharmaceutical compositions of an antibody molecule, vectors which direct the expression of high levels of fusion

15 protein products that are readily purified may be desirable. Such vectors include, but are not limited, to the *E. coli* expression vector pUR278 (Ruther et al., *EMBO J.* 2:1791 (1983)), in which the antibody coding sequence may be ligated individually into the vector in frame with the *lac Z* coding region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, *Nucleic Acids Res.* 13:3101-3109 (1985); Van Heeke & Schuster, *J. Biol. Chem.* 24:5503-5509 (1989)); and the

20 like. pGEX vectors may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption and binding to matrix glutathione-agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target gene product can be

25 released from the GST moiety.

In an insect system, *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes. The virus grows in *Spodoptera frugiperda* cells. The antibody coding sequence may be cloned individually into non-essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the

30 polyhedrin promoter).

In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, the antibody coding sequence of interest may be ligated to an adenovirus transcription/translation control complex, e.g., the late promoter and tripartite leader sequence. This chimeric gene may then be inserted in the

35 adenovirus genome by *in vitro* or *in vivo* recombination. Insertion in a non-essential region of the viral genome (e.g., region E1 or E3) will result in a recombinant virus that is viable and capable of expressing the antibody molecule in infected hosts. (e.g., see Logan & Shenk, *Proc. Natl. Acad.*

Sci. USA 81:355-359 (1984)). Specific initiation signals may also be required for efficient translation of inserted antibody coding sequences. These signals include the ATG initiation codon and adjacent sequences. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous
5 translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, etc. (see Bittner et al., Methods in Enzymol. 153:51-544 (1987)).

In addition, a host cell strain may be chosen which modulates the expression of the
10 inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products may be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and
15 processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERY, BHK, Hela, COS, MDCK, 293, 3T3, WI38, and in particular, breast cancer cell lines such as, for example, BT483, Hs578T, HTB2, BT20 and T47D, and normal
20 mammary gland cell line such as, for example, CRL7030 and Hs578Bst.

For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express the antibody molecule may be engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (e.g., promoter,
25 enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned
30 and expanded into cell lines. This method may advantageously be used to engineer cell lines which express the antibody molecule. Such engineered cell lines may be particularly useful in screening and evaluation of compounds that interact directly or indirectly with the antibody molecule.

A number of selection systems may be used, including but not limited to the herpes
35 simplex virus thymidine kinase (Wigler et al., Cell 11:223 (1977)), hypoxanthine-guanine phosphoribosyltransferase (Szybalska & Szybalski, Proc. Natl. Acad. Sci. USA 48:202 (1992)), and adenine phosphoribosyltransferase (Lowy et al., Cell 22:817 (1980)) genes can be employed

in tk-, hgp^rt- or ap^rt- cells, respectively. Also, antimetabolite resistance can be used as the basis of selection for the following genes: dhfr, which confers resistance to methotrexate (Wigler et al., Natl. Acad. Sci. USA 77:357 (1980); O'Hare et al., Proc. Natl. Acad. Sci. USA 78:1527 (1981)); gpt, which confers resistance to mycophenolic acid (Mulligan & Berg, Proc. Natl. Acad. Sci. USA 78:2072 (1981)); neo, which confers resistance to the aminoglycoside G-418 Clinical Pharmacy 12:488-505; Wu and Wu, Biotherapy 3:87-95 (1991); Tolstoshev, Ann. Rev. Pharmacol. Toxicol. 32:573-596 (1993); Mulligan, Science 260:926-932 (1993); and Morgan and Anderson, Ann. Rev. Biochem. 62:191-217 (1993); May, 1993, TIB TECH 11(5):155-215 (1993)); and hyg^r, which confers resistance to hygromycin (Santerre et al., Gene 30:147 (1984)). Methods commonly known in the art of recombinant DNA technology may be routinely applied to select the desired recombinant clone, and such methods are described, for example, in Ausubel et al. (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993); Kriegler, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990); and in Chapters 12 and 13, Dracopoli et al. (eds), Current Protocols in Human Genetics, John Wiley & Sons, NY (1994); Colberre-Garapin et al., J. Mol. Biol. 150:1 (1981), which are incorporated by reference herein in their entireties.

The expression levels of an antibody molecule can be increased by vector amplification (for a review, see Bebbington and Hentschel, The use of vectors based on gene amplification for the expression of cloned genes in mammalian cells in DNA cloning, Vol.3. (Academic Press, New York, 1987)). When a marker in the vector system expressing antibody is amplifiable, increase in the level of inhibitor present in culture of host cell will increase the number of copies of the marker gene. Since the amplified region is associated with the antibody gene, production of the antibody will also increase (Crouse et al., Mol. Cell. Biol. 3:257 (1983)).

Vectors which use glutamine synthase (GS) or DHFR as the selectable markers can be amplified in the presence of the drugs methionine sulphoximine or methotrexate, respectively. An advantage of glutamine synthase based vectors are the availability of cell lines (e.g., the murine myeloma cell line, NS0) which are glutamine synthase negative. Glutamine synthase expression systems can also function in glutamine synthase expressing cells (e.g. Chinese Hamster Ovary (CHO) cells) by providing additional inhibitor to prevent the functioning of the endogenous gene. A glutamine synthase expression system and components thereof are detailed in PCT publications: WO87/04462; WO86/05807; WO89/01036; WO89/10404; and WO91/06657 which are incorporated in their entireties by reference herein. Additionally, glutamine synthase expression vectors that may be used according to the present invention are commercially available from suppliers, including, for example Lonza Biologics, Inc. (Portsmouth, NH). Expression and production of monoclonal antibodies using a GS expression system in murine myeloma cells is described in Bebbington *et al.*, *Bio/technology* 10:169(1992) and in Biblia and Robinson *Biotechnol. Prog.* 11:1 (1995) which are incorporated in their entireties by reference herein.

The host cell may be co-transfected with two expression vectors of the invention, the first vector encoding a heavy chain derived polypeptide and the second vector encoding a light chain derived polypeptide. The two vectors may contain identical selectable markers which enable equal expression of heavy and light chain polypeptides. Alternatively, a single vector may be used which encodes, and is capable of expressing, both heavy and light chain polypeptides. In such situations, the light chain should be placed before the heavy chain to avoid an excess of toxic free heavy chain (Proudfoot, Nature 322:52 (1986); Kohler, Proc. Natl. Acad. Sci. USA 77:2197 (1980)). The coding sequences for the heavy and light chains may comprise cDNA or genomic DNA.

Once an antibody molecule of the invention has been produced by an animal, chemically synthesized, or recombinantly expressed, it may be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (e.g., ion exchange, affinity, particularly by affinity for the specific antigen after Protein A, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for the purification of proteins. In addition, the antibodies of the present invention or fragments thereof can be fused to heterologous polypeptide sequences described herein or otherwise known in the art, to facilitate purification.

The present invention encompasses antibodies recombinantly fused or chemically conjugated (including both covalently and non-covalently conjugations) to a polypeptide (or portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention to generate fusion proteins. The fusion does not necessarily need to be direct, but may occur through linker sequences. The antibodies may be specific for antigens other than polypeptides (or portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention. For example, antibodies may be used to target the polypeptides of the present invention to particular cell types, either in vitro or *in vivo*, by fusing or conjugating the polypeptides of the present invention to antibodies specific for particular cell surface receptors. Antibodies fused or conjugated to the polypeptides of the present invention may also be used in in vitro immunoassays and purification methods using methods known in the art. See e.g., Harbor et al., *supra*, and PCT publication WO 93/21232; EP 439,095; Naramura et al., Immunol. Lett. 39:91-99 (1994); U.S. Patent 5,474,981; Gillies et al., PNAS 89:1428-1432 (1992); Fell et al., J. Immunol. 146:2446-2452 (1991), which are incorporated by reference in their entireties.

The present invention further includes compositions comprising the polypeptides of the present invention fused or conjugated to antibody domains other than the variable regions. For example, the polypeptides of the present invention may be fused or conjugated to an antibody Fc region, or portion thereof. The antibody portion fused to a polypeptide of the present invention may comprise the constant region, hinge region, CH1 domain, CH2 domain, and CH3 domain or

any combination of whole domains or portions thereof. The polypeptides may also be fused or conjugated to the above antibody portions to form multimers. For example, Fc portions fused to the polypeptides of the present invention can form dimers through disulfide bonding between the Fc portions. Higher multimeric forms can be made by fusing the polypeptides to portions of IgA and IgM. Methods for fusing or conjugating the polypeptides of the present invention to antibody portions are known in the art. See, e.g., U.S. Patent Nos. 5,336,603; 5,622,929; 5,359,046; 5,349,053; 5,447,851; 5,112,946; EP 307,434; EP 367,166; PCT publications WO 96/04388; WO 91/06570; Ashkenazi et al., Proc. Natl. Acad. Sci. USA 88:10535-10539 (1991); Zheng et al., J. Immunol. 154:5590-5600 (1995); and Vil et al., Proc. Natl. Acad. Sci. USA 89:11337-11341 (1992) (said references incorporated by reference in their entireties).

As discussed, *supra*, the polypeptides corresponding to a polypeptide, polypeptide fragment, or a variant of SEQ ID NO:Y may be fused or conjugated to the above antibody portions to increase the *in vivo* half life of the polypeptides or for use in immunoassays using methods known in the art. Further, the polypeptides corresponding to SEQ ID NO:Y may be fused or conjugated to the above antibody portions to facilitate purification. One reported example describes chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. See EP 394,827; and Traunecker et al., Nature 331:84-86 (1988). The polypeptides of the present invention fused or conjugated to an antibody having disulfide-linked dimeric structures (due to the IgG) may also be more efficient in binding and neutralizing other molecules, than the monomeric secreted protein or protein fragment alone. See, for example, Fountoulakis et al., J. Biochem. 270:3958-3964 (1995). In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. See, for example, EP A 232,262. Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, Bennett et al., J. Molecular Recognition 8:52-58 (1995); Johanson et al., J. Biol. Chem. 270:9459-9471 (1995)).

Moreover, the antibodies or fragments thereof of the present invention can be fused to marker sequences, such as a peptide to facilitate purification. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Other peptide tags useful for purification include, but are not limited to, the "HA" tag, which

corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., Cell 37:767 (1984)) and the "flag" tag.

The present invention further encompasses antibodies or fragments thereof conjugated to a diagnostic or therapeutic agent. The antibodies can be used diagnostically to, for example, monitor the development or progression of a tumor as part of a clinical testing procedure to, e.g., determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, radioactive materials, positron emitting metals using various positron emission tomographies, and nonradioactive paramagnetic metal ions. The detectable substance may be coupled or conjugated either directly to the antibody (or fragment thereof) or indirectly, through an intermediate (such as, for example, a linker known in the art) using techniques known in the art. See, for example, U.S. Patent No. 4,741,900 for metal ions which can be conjugated to antibodies for use as diagnostics according to the present invention. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin; and examples of suitable radioactive material include ^{125}I , ^{131}I , ^{111}In or ^{99}Tc .

Further, an antibody or fragment thereof may be conjugated to a therapeutic moiety such as a cytotoxin, e.g., a cytostatic or cytotoxic agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example, ^{213}Bi . A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells. Examples include paclitaxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, teniposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (e.g., mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine and vinblastine).

The conjugates of the invention can be used for modifying a given biological response, the therapeutic agent or drug moiety is not to be construed as limited to classical chemical therapeutic

agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a protein such as tumor necrosis factor, α -interferon, β -interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator, an apoptotic agent, e.g., TNF- α , TNF- β , AIM I (See, International Publication No. WO 97/33899), AIM II (See, International Publication No. WO 97/34911), Fas Ligand (Takahashi *et al.*, *Int. Immunol.*, 6:1567-1574 (1994)), VEGI (See, International Publication No. WO 99/23105), a thrombotic agent or an anti-angiogenic agent, e.g., angiostatin or endostatin; or, biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors.

Antibodies may also be attached to solid supports, which are particularly useful for immunoassays or purification of the target antigen. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

Techniques for conjugating such therapeutic moiety to antibodies are well known. See, for example, Arnon *et al.*, "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in *Monoclonal Antibodies And Cancer Therapy*, Reisfeld *et al.* (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom *et al.*, "Antibodies For Drug Delivery", in *Controlled Drug Delivery* (2nd Ed.), Robinson *et al.* (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in *Monoclonal Antibodies '84: Biological And Clinical Applications*, Pinchera *et al.* (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in *Monoclonal Antibodies For Cancer Detection And Therapy*, Baldwin *et al.* (eds.), pp. 303-16 (Academic Press 1985), and Thorpe *et al.*, "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", *Immunol. Rev.* 62:119-58 (1982).

Alternatively, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate as described by Segal in U.S. Patent No. 4,676,980, which is incorporated herein by reference in its entirety.

An antibody, with or without a therapeutic moiety conjugated to it, administered alone or in combination with cytotoxic factor(s) and/or cytokine(s) can be used as a therapeutic.

Immunophenotyping

The antibodies of the invention may be utilized for immunophenotyping of cell lines and biological samples. Translation products of the gene of the present invention may be useful as cell-specific markers, or more specifically as cellular markers that are differentially expressed at various stages of differentiation and/or maturation of particular cell types. Monoclonal antibodies

directed against a specific epitope, or combination of epitopes, will allow for the screening of cellular populations expressing the marker. Various techniques can be utilized using monoclonal antibodies to screen for cellular populations expressing the marker(s), and include magnetic separation using antibody-coated magnetic beads, "panning" with antibody attached to a solid matrix (i.e., plate), and flow cytometry (See, e.g., U.S. Patent 5,985,660; and Morrison *et al.*, *Cell*, 96:737-49 (1999)).

These techniques allow for the screening of particular populations of cells, such as might be found with hematological malignancies (i.e. minimal residual disease (MRD) in acute leukemic patients) and "non-self" cells in transplantations to prevent Graft-versus-Host Disease (GVHD). Alternatively, these techniques allow for the screening of hematopoietic stem and progenitor cells capable of undergoing proliferation and/or differentiation, as might be found in human umbilical cord blood.

Assays For Antibody Binding

The antibodies of the invention may be assayed for immunospecific binding by any method known in the art. The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, and protein A immunoassays, to name but a few. Such assays are routine and well known in the art (see, e.g., Ausubel *et al.*, eds, 1994, *Current Protocols in Molecular Biology*, Vol. 1, John Wiley & Sons, Inc., New York, which is incorporated by reference herein in its entirety). Exemplary immunoassays are described briefly below (but are not intended by way of limitation).

Immunoprecipitation protocols generally comprise lysing a population of cells in a lysis buffer such as RIPA buffer (1% NP-40 or Triton X- 100, 1% sodium deoxycholate, 0.1% SDS, 0.15 M NaCl, 0.01 M sodium phosphate at pH 7.2, 1% Trasylol) supplemented with protein phosphatase and/or protease inhibitors (e.g., EDTA, PMSF, aprotinin, sodium vanadate), adding the antibody of interest to the cell lysate, incubating for a period of time (e.g., 1-4 hours) at 4° C, adding protein A and/or protein G sepharose beads to the cell lysate, incubating for about an hour or more at 4° C, washing the beads in lysis buffer and resuspending the beads in SDS/sample buffer. The ability of the antibody of interest to immunoprecipitate a particular antigen can be assessed by, e.g., western blot analysis. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the binding of the antibody to an antigen and decrease the background (e.g., pre-clearing the cell lysate with sepharose beads). For further discussion

regarding immunoprecipitation protocols see, e.g., Ausubel et al., eds., (1994), Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, section 10.16.1.

Western blot analysis generally comprises preparing protein samples, electrophoresis of the protein samples in a polyacrylamide gel (e.g., 8%- 20% SDS-PAGE depending on the molecular weight of the antigen), transferring the protein sample from the polyacrylamide gel to a membrane such as nitrocellulose, PVDF or nylon, blocking the membrane in blocking solution (e.g., PBS with 3% BSA or non-fat milk), washing the membrane in washing buffer (e.g., PBS-Tween 20), blocking the membrane with primary antibody (the antibody of interest) diluted in blocking buffer, washing the membrane in washing buffer, blocking the membrane with a secondary antibody (which recognizes the primary antibody, e.g., an anti-human antibody) conjugated to an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) or radioactive molecule (e.g., ³²P or ¹²⁵I) diluted in blocking buffer, washing the membrane in wash buffer, and detecting the presence of the antigen. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected and to reduce the background noise. For further discussion regarding western blot protocols see, e.g., Ausubel et al, eds, (1994), Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, section 10.8.1.

ELISAs comprise preparing antigen, coating the well of a 96 well microtiter plate with the antigen, adding the antibody of interest conjugated to a detectable compound such as an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) to the well and incubating for a period of time, and detecting the presence of the antigen. In ELISAs the antibody of interest does not have to be conjugated to a detectable compound; instead, a second antibody (which recognizes the antibody of interest) conjugated to a detectable compound may be added to the well. Further, instead of coating the well with the antigen, the antibody may be coated to the well. In this case, a second antibody conjugated to a detectable compound may be added following the addition of the antigen of interest to the coated well. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected as well as other variations of ELISAs known in the art. For further discussion regarding ELISAs see, e.g., Ausubel et al, eds, (1994), Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, section 11.2.1.

The binding affinity of an antibody to an antigen and the off-rate of an antibody-antigen interaction can be determined by competitive binding assays. One example of a competitive binding assay is a radioimmunoassay comprising the incubation of labeled antigen (e.g., ³H or ¹²⁵I) with the antibody of interest in the presence of increasing amounts of unlabeled antigen, and the detection of the antibody bound to the labeled antigen. The affinity of the antibody of interest for a particular antigen and the binding off-rates can be determined from the data by scatchard plot analysis. Competition with a second antibody can also be determined using radioimmunoassays.

In this case, the antigen is incubated with antibody of interest conjugated to a labeled compound (e.g., ³H or ¹²⁵I) in the presence of increasing amounts of an unlabeled second antibody.

Antibodies of the invention may be characterized using immunocytochemistry methods on cells (e.g., mammalian cells, such as CHO cells) transfected with a vector enabling the expression of an antigen or with vector alone using techniques commonly known in the art. Antibodies that bind antigen transfected cells, but not vector-only transfected cells, are antigen specific.

Therapeutic Uses

Table 1D also provides information regarding biological activities and preferred therapeutic uses (i.e. see, "Preferred Indications" column) for polynucleotides and polypeptides of the invention (including antibodies, agonists, and/or antagonists thereof). Table 1D also provides information regarding assays which may be used to test polynucleotides and polypeptides of the invention (including antibodies, agonists, and/or antagonists thereof) for the corresponding biological activities. The first column ("Gene No.") provides the gene number in the application for each clone identifier. The second column ("cDNA ATCC Deposit No:Z") provides the unique clone identifier for each clone as previously described and indicated in Table 1A, Table 1B, and Table 1C. The third column ("AA SEQ ID NO:Y") indicates the Sequence Listing SEQ ID Number for polypeptide sequences encoded by the corresponding cDNA clones (also as indicated in Table 1A, Table 1B, and Table 2). The fourth column ("Biological Activity") indicates a biological activity corresponding to the indicated polypeptides (or polynucleotides encoding said polypeptides). The fifth column ("Exemplary Activity Assay") further describes the corresponding biological activity and also provides information pertaining to the various types of assays which may be performed to test, demonstrate, or quantify the corresponding biological activity.

The present invention is further directed to antibody-based therapies which involve administering antibodies of the invention to an animal, preferably a mammal, and most preferably a human, patient for treating one or more of the disclosed diseases, disorders, or conditions. Therapeutic compounds of the invention include, but are not limited to, antibodies of the invention (including fragments, analogs and derivatives thereof as described herein) and nucleic acids encoding antibodies of the invention (including fragments, analogs and derivatives thereof and anti-idiotypic antibodies as described herein). The antibodies of the invention can be used to detect, prevent, diagnose, prognosticate, treat, and/or ameliorate diseases, disorders or conditions associated with aberrant expression and/or activity of a polypeptide of the invention, including, but not limited to, cancer and other hyperproliferative diseases and disorders. The treatment and/or prevention of cancer and other hyperproliferative diseases and disorders associated with aberrant expression and/or activity of a polypeptide of the invention includes, but is not limited to, alleviating symptoms associated with cancer and other hyperproliferative diseases and disorders.

Antibodies of the invention may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

In a specific and preferred embodiment, the present invention is directed to antibody-based therapies which involve administering antibodies of the invention to an animal, preferably a mammal, and most preferably a human, patient for treating cancer and other hyperproliferative diseases and disorders. Therapeutic compounds of the invention include, but are not limited to, antibodies of the invention (e.g., antibodies directed to the full length protein expressed on the cell surface of a mammalian cell; antibodies directed to an epitope of a polypeptide of the invention (such as, for example, a predicted linear epitope shown in column 7 of Table 1B.1; or a conformational epitope, including fragments, analogs and derivatives thereof as described herein) and nucleic acids encoding antibodies of the invention (including fragments, analogs and derivatives thereof and anti-idiotypic antibodies as described herein). The antibodies of the invention can be used to detect, diagnose, prevent, treat, prognosticate, and/or ameliorate cancer and other hyperproliferative diseases, disorders or conditions associated with aberrant expression and/or activity of a polypeptide of the invention. The treatment and/or prevention of cancer and other hyperproliferative diseases, disorders, or conditions associated with aberrant expression and/or activity of a polypeptide of the invention includes, but is not limited to, alleviating symptoms associated with those diseases, disorders or conditions. Antibodies of the invention may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

A summary of the ways in which the antibodies of the present invention may be used therapeutically includes binding polynucleotides or polypeptides of the present invention locally or systemically in the body or by direct cytotoxicity of the antibody, e.g. as mediated by complement (CDC) or by effector cells (ADCC). Some of these approaches are described in more detail below. Armed with the teachings provided herein, one of ordinary skill in the art will know how to use the antibodies of the present invention for diagnostic, monitoring or therapeutic purposes without undue experimentation.

The antibodies of this invention may be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors (such as, e.g., IL-2, IL-3 and IL-7), for example, which serve to increase the number or activity of effector cells which interact with the antibodies.

The antibodies of the invention may be administered alone or in combination with other types of treatments (e.g., radiation therapy, chemotherapy, hormonal therapy, immunotherapy and anti-tumor agents). Generally, administration of products of a species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, human antibodies, fragments derivatives, analogs, or nucleic acids, are administered to a human patient for therapy or prophylaxis.

It is preferred to use high affinity and/or potent *in vivo* inhibiting and/or neutralizing antibodies against polypeptides or polynucleotides of the present invention, fragments or regions thereof, for both immunoassays directed to and therapy of cancer and other hyperproliferative diseases and disorders related to polynucleotides or polypeptides, including fragments thereof, of the present invention. Such antibodies, fragments, or regions, will preferably have an affinity for polynucleotides or polypeptides of the invention, including fragments thereof. Preferred binding affinities include those with a dissociation constant or K_d less than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, and 10^{-15} M.

Gene Therapy

In a specific embodiment, nucleic acids comprising sequences encoding antibodies or functional derivatives thereof, are administered to treat, inhibit or prevent cancer and other hyperproliferative disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention, by way of gene therapy. Gene therapy refers to therapy performed by the administration to a subject of an expressed or expressible nucleic acid. In this embodiment of the invention, the nucleic acids produce their encoded protein that mediates a therapeutic effect.

Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

For general reviews of the methods of gene therapy, see Goldspiel et al., *Clinical Pharmacy* 12:488-505 (1993); Wu and Wu, *Biotherapy* 3:87-95 (1991); Tolstoshev, *Ann. Rev. Pharmacol. Toxicol.* 32:573-596 (1993); Mulligan, *Science* 260:926-932 (1993); and Morgan and Anderson, *Ann. Rev. Biochem.* 62:191-217 (1993); May, *TIBTECH* 11(5):155-215 (1993). Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al. (eds.), *Current Protocols in Molecular Biology*, John Wiley & Sons, NY (1993); and Kriegler, *Gene Transfer and Expression, A Laboratory Manual*, Stockton Press, NY (1990).

In a preferred embodiment, the compound comprises nucleic acid sequences encoding an antibody, said nucleic acid sequences being part of expression vectors that express the antibody or fragments or chimeric proteins or heavy or light chains thereof in a suitable host. In particular, such nucleic acid sequences have promoters operably linked to the antibody coding region, said promoter being inducible or constitutive, and, optionally, tissue-specific. In another particular embodiment, nucleic acid molecules are used in which the antibody coding sequences and any other desired sequences are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intrachromosomal expression of the antibody

encoding nucleic acids (Koller and Smithies, Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); Zijlstra et al., Nature 342:435-438 (1989)). In specific embodiments, the expressed antibody molecule is a single chain antibody; alternatively, the nucleic acid sequences include sequences encoding both the heavy and light chains, or fragments thereof, of the antibody.

5 Delivery of the nucleic acids into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid-carrying vectors, or indirect, in which case, cells are first transformed with the nucleic acids *in vitro*, then transplanted into the patient. These two approaches are known, respectively, as *in vivo* or *ex vivo* gene therapy.

10 In a specific embodiment, the nucleic acid sequences are directly administered *in vivo*, where it is expressed to produce the encoded product. This can be accomplished by any of numerous methods known in the art, e.g., by constructing them as part of an appropriate nucleic acid expression vector and administering it so that they become intracellular, e.g., by infection using defective or attenuated retrovirals or other viral vectors (see U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle bombardment (e.g., a gene gun; 15 Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, encapsulation in liposomes, microparticles, or microcapsules, or by administering them in linkage to a peptide which is known to enter the nucleus, by administering it in linkage to a ligand subject to receptor-mediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)) (which can be used to target cell types specifically expressing the receptors), etc. In another 20 embodiment, nucleic acid-ligand complexes can be formed in which the ligand comprises a fusogenic viral peptide to disrupt endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted *in vivo* for cell specific uptake and expression, by targeting a specific receptor (see, e.g., PCT Publications WO 92/06180; WO 92/22635; WO92/20316; WO93/14188, WO 93/20221). Alternatively, the nucleic acid can 25 be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); Zijlstra et al., Nature 342:435-438 (1989)).

 In a specific embodiment, viral vectors that contains nucleic acid sequences encoding an antibody of the invention are used. For example, a retroviral vector can be used (see Miller et al., 30 Meth. Enzymol. 217:581-599 (1993)). These retroviral vectors contain the components necessary for the correct packaging of the viral genome and integration into the host cell DNA. The nucleic acid sequences encoding the antibody to be used in gene therapy are cloned into one or more vectors, which facilitates delivery of the gene into a patient. More detail about retroviral vectors can be found in Boesen et al., Biotherapy 6:291-302 (1994), which describes the use of a 35 retroviral vector to deliver the *mdr1* gene to hematopoietic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are: Clowes et al., J. Clin. Invest. 93:644-651 (1994); Kiem et al., Blood 83:1467-

1473 (1994); Salmons and Gunzberg, *Human Gene Therapy* 4:129-141 (1993); and Grossman and Wilson, *Curr. Opin. in Genetics and Devel.* 3:110-114 (1993).

Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are liver, the central nervous system, endothelial cells, and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, *Current Opinion in Genetics and Development* 3:499-503 (1993) present a review of adenovirus-based gene therapy. Bout et al., *Human Gene Therapy* 5:3-10 (1994) demonstrated the use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., *Science* 252:431-434 (1991); Rosenfeld et al., *Cell* 68:143-155 (1992); Mastrangeli et al., *J. Clin. Invest.* 91:225-234 (1993); PCT Publication WO94/12649; and Wang, et al., *Gene Therapy* 2:775-783 (1995). In a preferred embodiment, adenovirus vectors are used.

Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., *Proc. Soc. Exp. Biol. Med.* 204:289-300 (1993); U.S. Patent No. 5,436,146).

Another approach to gene therapy involves transferring a gene to cells in tissue culture by such methods as electroporation, lipofection, calcium phosphate mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those cells that have taken up and are expressing the transferred gene. Those cells are then delivered to a patient.

In this embodiment, the nucleic acid is introduced into a cell prior to administration *in vivo* of the resulting recombinant cell. Such introduction can be carried out by any method known in the art, including but not limited to transfection, electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes into cells (see, e.g., Loeffler and Behr, *Meth. Enzymol.* 217:599-618 (1993); Cohen et al., *Meth. Enzymol.* 217:618-644 (1993); Cline, *Pharmac. Ther.* 29:69-92m (1985) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably heritable and expressible by its cell progeny.

The resulting recombinant cells can be delivered to a patient by various methods known in the art. Recombinant blood cells (e.g., hematopoietic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes; blood cells such as T lymphocytes, B lymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, granulocytes; various stem or progenitor cells, in particular hematopoietic stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

In a preferred embodiment, the cell used for gene therapy is autologous to the patient.

In an embodiment in which recombinant cells are used in gene therapy, nucleic acid sequences encoding an antibody are introduced into the cells such that they are expressible by the cells or their progeny, and the recombinant cells are then administered *in vivo* for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained *in vitro* can potentially be used in accordance with this embodiment of the present invention (see e.g. PCT Publication WO 94/08598; Stemple and Anderson, *Cell* 71:973-985 (1992); Rheinwald, *Meth. Cell Bio.* 21A:229 (1980); and Pittelkow and Scott, *Mayo Clinic Proc.* 61:771 (1986)).

In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that expression of the nucleic acid is controllable by the presence or absence of an appropriate inducer of transcription.

Demonstration of Therapeutic or Prophylactic Activity

The compounds or pharmaceutical compositions of the invention are preferably tested *in vitro*, and then *in vivo* for the desired therapeutic or prophylactic activity, prior to use in humans. For example, *in vitro* assays to demonstrate the therapeutic or prophylactic utility of a compound or pharmaceutical composition include, the effect of a compound on a cell line or a patient tissue sample. The effect of the compound or composition on the cell line and/or tissue sample can be determined utilizing techniques known to those of skill in the art including, but not limited to, rosette formation assays and cell lysis assays. In accordance with the invention, *in vitro* assays which can be used to determine whether administration of a specific compound is indicated, include *in vitro* cell culture assays in which a patient tissue sample is grown in culture, and exposed to or otherwise administered a compound, and the effect of such compound upon the tissue sample is observed.

Therapeutic/Prophylactic Administration and Composition

The invention provides methods of treatment, inhibition and prophylaxis by administration to a subject of an effective amount of a compound or pharmaceutical composition of the invention, preferably a polypeptide or antibody of the invention. In a preferred embodiment, the compound is substantially purified (e.g., substantially free from substances that limit its effect or produce

undesired side-effects). The subject is preferably an animal, including but not limited to animals such as cows, pigs, horses, chickens, cats, dogs, etc., and is preferably a mammal, and most preferably human.

Formulations and methods of administration that can be employed when the compound
5 comprises a nucleic acid or an immunoglobulin are described above; additional appropriate formulations and routes of administration can be selected from among those described herein below.

Various delivery systems are known and can be used to administer a compound of the invention, e.g., encapsulation in liposomes, microparticles, microcapsules, recombinant cells
10 capable of expressing the compound, receptor-mediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)), construction of a nucleic acid as part of a retroviral or other vector, etc. Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds or compositions may be administered by any convenient route, for example by infusion or bolus
15 injection, by absorption through epithelial or mucocutaneous linings (e.g., oral mucosa, rectal and intestinal mucosa, etc.) and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, it may be desirable to introduce the pharmaceutical compounds or compositions of the invention into the central nervous system by any suitable route, including intraventricular and intrathecal injection; intraventricular injection
20 may be facilitated by an intraventricular catheter, for example, attached to a reservoir, such as an Ommaya reservoir. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

In a specific embodiment, it may be desirable to administer the pharmaceutical compounds or compositions of the invention locally to the area in need of treatment; this may be
25 achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. Preferably, when administering a protein, including an antibody, of the invention, care must be
30 taken to use materials to which the protein does not absorb.

In another embodiment, the compound or composition can be delivered in a vesicle, in particular a liposome (see Langer, Science 249:1527-1533 (1990); Treat et al., in Liposomes in the Therapy of Infectious Disease and Cancer, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 353-365 (1989); Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*)

35 In yet another embodiment, the compound or composition can be delivered in a controlled release system. In one embodiment, a pump may be used (see Langer, *supra*; Sefton, CRC Crit. Ref. Biomed. Eng. 14:201 (1987); Buchwald et al., Surgery 88:507 (1980); Saudek et al., N. Engl.

J. Med. 321:574 (1989)). In another embodiment, polymeric materials can be used (see Medical Applications of Controlled Release, Langer and Wise (eds.), CRC Pres., Boca Raton, Florida (1974); Controlled Drug Bioavailability, Drug Product Design and Performance, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, J., Macromol. Sci. Rev. Macromol. Chem. 23:61 (1983); see also Levy et al., Science 228:190 (1985); During et al., Ann. Neurol. 25:351 (1989); Howard et al., J.Neurosurg. 71:105 (1989)). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, e.g., the brain, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in Medical Applications of Controlled Release, *supra*, vol. 2, pp. 115-138 (1984)).

Other controlled release systems are discussed in the review by Langer (Science 249:1527-1533 (1990)).

In a specific embodiment where the compound of the invention is a nucleic acid encoding a protein, the nucleic acid can be administered *in vivo* to promote expression of its encoded protein, by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by use of a retroviral vector (see U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, or by administering it in linkage to a homeobox- like peptide which is known to enter the nucleus (see e.g., Joliot et al., Proc. Natl. Acad. Sci. USA 88:1864-1868 (1991)), etc. Alternatively, a nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination.

The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules,

powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the compound, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

In a preferred embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

The compounds of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with anions such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with cations such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc.

The amount of the compound of the invention which will be effective in the treatment, inhibition and prevention of a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention can be determined by standard clinical techniques. In addition, *in vitro* assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. Effective doses may be extrapolated from dose-response curves derived from *in vitro* or animal model test systems.

For antibodies, the dosage administered to a patient is typically 0.1 mg/kg to 100 mg/kg of the patient's body weight. Preferably, the dosage administered to a patient is between 0.1 mg/kg and 20 mg/kg of the patient's body weight, more preferably 1 mg/kg to 10 mg/kg of the patient's body weight. Generally, human antibodies have a longer half-life within the human body than

antibodies from other species due to the immune response to the foreign polypeptides. Thus, lower dosages of human antibodies and less frequent administration is often possible. Further, the dosage and frequency of administration of antibodies of the invention may be reduced by enhancing uptake and tissue penetration (e.g., into the brain) of the antibodies by modifications such as, for example, lipidation.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

Diagnosis and Imaging

Labeled antibodies, and derivatives and analogs thereof, which specifically bind to a polypeptide of interest can be used for diagnostic purposes to detect, diagnose, prognosticate, or monitor cancer and other hyperproliferative diseases, disorders, and/or conditions associated with the aberrant expression and/or activity of a polypeptide of the invention. The invention provides for the detection of aberrant expression of a polypeptide of interest, comprising (a) assaying the expression of the polypeptide of interest in cells or body fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of aberrant expression.

The invention provides a diagnostic assay for diagnosing cancer and other hyperproliferative disease or disorder, comprising (a) assaying the expression of the polypeptide of interest in cells or body fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a particular cancer or other hyperproliferative disease or disorder. With respect to cancer and other hyperproliferative diseases and disorders, the presence of a relatively high amount of transcript in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer or other hyperproliferative disease.

Antibodies of the invention can be used to assay protein levels in a biological sample using classical immunohistological methods known to those of skill in the art (e.g., see Jalkanen

et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen et al., J. Cell . Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose
5 oxidase; radioisotopes, such as iodine (125I, 121I), carbon (14C), sulfur (35S), tritium (3H), indium (112In), and technetium (99Tc); luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

One facet of the invention is the detection and diagnosis of a disease or disorder associated with aberrant expression of a polypeptide of interest in an animal, preferably a mammal and most
10 preferably a human. In one embodiment, diagnosis comprises: a) administering (for example, parenterally, subcutaneously, or intraperitoneally) to a subject an effective amount of a labeled molecule which specifically binds to the polypeptide of interest; b) waiting for a time interval following the administering for permitting the labeled molecule to preferentially concentrate at sites in the subject where the polypeptide is expressed (and for unbound labeled molecule to be
15 cleared to background level); c) determining background level; and d) detecting the labeled molecule in the subject, such that detection of labeled molecule above the background level indicates that the subject has a particular disease or disorder associated with aberrant expression of the polypeptide of interest. Background level can be determined by various methods including, comparing the amount of labeled molecule detected to a standard value previously determined for
20 a particular system.

It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of 99mTc. The labeled antibody or antibody fragment will then
25 preferentially accumulate at the location of cells which contain the specific protein. *In vivo* tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982)).

Depending on several variables, including the type of label used and the mode of
30 administration, the time interval following the administration for permitting the labeled molecule to preferentially concentrate at sites in the subject and for unbound labeled molecule to be cleared to background level is 6 to 48 hours or 6 to 24 hours or 6 to 12 hours. In another embodiment the time interval following administration is 5 to 20 days or 5 to 10 days.

In an embodiment, monitoring of the disease or disorder is carried out by repeating the
35 method for diagnosing the disease or disease, for example, one month after initial diagnosis, six months after initial diagnosis, one year after initial diagnosis, etc.

Presence of the labeled molecule can be detected in the patient using methods known in the art for *in vivo* scanning. These methods depend upon the type of label used. Skilled artisans will be able to determine the appropriate method for detecting a particular label. Methods and devices that may be used in the diagnostic methods of the invention include, but are not limited to, computed tomography (CT), whole body scan such as position emission tomography (PET),
5 magnetic resonance imaging (MRI), and sonography.

In a specific embodiment, the molecule is labeled with a radioisotope and is detected in the patient using a radiation responsive surgical instrument (Thurston et al., U.S. Patent No. 5,441,050). In another embodiment, the molecule is labeled with a fluorescent compound and is
10 detected in the patient using a fluorescence responsive scanning instrument. In another embodiment, the molecule is labeled with a positron emitting metal and is detected in the patient using positron emission-tomography. In yet another embodiment, the molecule is labeled with a paramagnetic label and is detected in a patient using magnetic resonance imaging (MRI).

15 *Kits*

The present invention provides kits that can be used in the above methods. In one embodiment, a kit comprises an antibody of the invention, preferably a purified antibody, in one or more containers. In a specific embodiment, the kits of the present invention contain a substantially isolated polypeptide comprising an epitope which is specifically immunoreactive with an antibody
20 included in the kit. Preferably, the kits of the present invention further comprise a control antibody which does not react with the polypeptide of interest. In another specific embodiment, the kits of the present invention contain a means for detecting the binding of an antibody to a polypeptide of interest (e.g., the antibody may be conjugated to a detectable substrate such as a fluorescent compound, an enzymatic substrate, a radioactive compound or a luminescent
25 compound, or a second antibody which recognizes the first antibody may be conjugated to a detectable substrate).

In another specific embodiment of the present invention, the kit is a diagnostic kit for use in screening serum containing antibodies specific against proliferative and/or cancerous polynucleotides and polypeptides. Such a kit may include a control antibody that does not react
30 with the polypeptide of interest. Such a kit may include a substantially isolated polypeptide antigen comprising an epitope which is specifically immunoreactive with at least one anti-polypeptide antigen antibody. Further, such a kit includes means for detecting the binding of said antibody to the antigen (e.g., the antibody may be conjugated to a fluorescent compound such as fluorescein or rhodamine which can be detected by flow cytometry). In specific embodiments, the
35 kit may include a recombinantly produced or chemically synthesized polypeptide antigen. The polypeptide antigen of the kit may also be attached to a solid support.

In a more specific embodiment the detecting means of the above-described kit includes a solid support to which said polypeptide antigen is attached. Such a kit may also include a non-attached reporter-labeled anti-human antibody. In this embodiment, binding of the antibody to the polypeptide antigen can be detected by binding of the said reporter-labeled antibody.

5 In an additional embodiment, the invention includes a diagnostic kit for use in screening serum containing antigens of the polypeptide of the invention. The diagnostic kit includes a substantially isolated antibody specifically immunoreactive with polypeptide or polynucleotide antigens, and means for detecting the binding of the polynucleotide or polypeptide antigen to the antibody. In one embodiment, the antibody is attached to a solid support. In a specific
10 embodiment, the antibody may be a monoclonal antibody. The detecting means of the kit may include a second, labeled monoclonal antibody. Alternatively, or in addition, the detecting means may include a labeled, competing antigen.

In one diagnostic configuration, test serum is reacted with a solid phase reagent having a surface-bound antigen obtained by the methods of the present invention. After binding with
15 specific antigen antibody to the reagent and removing unbound serum components by washing, the reagent is reacted with reporter-labeled anti-human antibody to bind reporter to the reagent in proportion to the amount of bound anti-antigen antibody on the solid support. The reagent is again washed to remove unbound labeled antibody, and the amount of reporter associated with the reagent is determined. Typically, the reporter is an enzyme which is detected by incubating the
20 solid phase in the presence of a suitable fluorometric, luminescent or colorimetric substrate (Sigma, St. Louis, MO).

The solid surface reagent in the above assay is prepared by known techniques for attaching protein material to solid support material, such as polymeric beads, dip sticks, 96-well plate or filter material. These attachment methods generally include non-specific adsorption of the protein
25 to the support or covalent attachment of the protein, typically through a free amine group, to a chemically reactive group on the solid support, such as an activated carboxyl, hydroxyl, or aldehyde group. Alternatively, streptavidin coated plates can be used in conjunction with biotinylated antigen(s).

Thus, the invention provides an assay system or kit for carrying out this diagnostic
30 method. The kit generally includes a support with surface-bound recombinant antigens, and a reporter-labeled anti-human antibody for detecting surface-bound anti-antigen antibody.

Uses of the Polynucleotides

35 Each of the polynucleotides identified herein can be used in numerous ways as reagents. The following description should be considered exemplary and utilizes known techniques.

The polynucleotides of the present invention are useful for chromosome identification. There exists an ongoing need to identify new chromosome markers, since few chromosome marking reagents, based on actual sequence data (repeat polymorphisms), are presently available. Each sequence is specifically targeted to and can hybridize with a particular location on an individual human chromosome, thus each polynucleotide of the present invention can routinely be used as a chromosome marker using techniques known in the art. Table 1B.1, column 8 provides the chromosome location of some of the polynucleotides of the invention.

Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably at least 15 bp (e.g., 15-25 bp) from the sequences shown in SEQ ID NO:X. Primers can optionally be selected using computer analysis so that primers do not span more than one predicted exon in the genomic DNA. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to SEQ ID NO:X will yield an amplified fragment.

Similarly, somatic hybrids provide a rapid method of PCR mapping the polynucleotides to particular chromosomes. Three or more clones can be assigned per day using a single thermal cycler. Moreover, sublocalization of the polynucleotides can be achieved with panels of specific chromosome fragments. Other gene mapping strategies that can be used include in situ hybridization, prescreening with labeled flow-sorted chromosomes, preselection by hybridization to construct chromosome specific-cDNA libraries, and computer mapping techniques (See, e.g., Shuler, Trends Biotechnol 16:456-459 (1998) which is hereby incorporated by reference in its entirety).

Precise chromosomal location of the polynucleotides can also be achieved using fluorescence in situ hybridization (FISH) of a metaphase chromosomal spread. This technique uses polynucleotides as short as 500 or 600 bases; however, polynucleotides 2,000-4,000 bp are preferred. For a review of this technique, see Verma et al., "Human Chromosomes: a Manual of Basic Techniques," Pergamon Press, New York (1988).

For chromosome mapping, the polynucleotides can be used individually (to mark a single chromosome or a single site on that chromosome) or in panels (for marking multiple sites and/or multiple chromosomes).

Thus, the present invention also provides a method for chromosomal localization which involves (a) preparing PCR primers from the polynucleotide sequences in Table 1B and/or Table 2 and SEQ ID NO:X and (b) screening somatic cell hybrids containing individual chromosomes.

The polynucleotides of the present invention would likewise be useful for radiation hybrid mapping, HAPPY mapping, and long range restriction mapping. For a review of these techniques and others known in the art, see, e.g. Dear, "Genome Mapping: A Practical Approach," IRL Press at Oxford University Press, London (1997); Aydin, J. Mol. Med. 77:691-694 (1999); Hacia et al., Mol. Psychiatry 3:483-492 (1998); Herrick et al., Chromosome Res. 7:409-423 (1999); Hamilton

et al., *Methods Cell Biol.* 62:265-280 (2000); and/or Ott, J. *Hered.* 90:68-70 (1999) each of which is hereby incorporated by reference in its entirety.

Once a polynucleotide has been mapped to a precise chromosomal location, the physical position of the polynucleotide can be used in linkage analysis. Linkage analysis establishes
5 coinheritance between a chromosomal location and presentation of a particular disease. (Disease mapping data are found, for example, in V. McKusick, *Mendelian Inheritance in Man* (available on line through Johns Hopkins University Welch Medical Library)). Column 9 of Table 1B.1 provides an OMIM reference identification number of diseases associated with the cytologic band disclosed in column 8 of Table 1B.1, as determined using techniques described herein and by
10 reference to Table 5. Assuming 1 megabase mapping resolution and one gene per 20 kb, a cDNA precisely localized to a chromosomal region associated with the disease could be one of 50-500 potential causative genes.

Thus, once coinheritance is established, differences in a polynucleotide of the invention and the corresponding gene between affected and unaffected individuals can be examined. First,
15 visible structural alterations in the chromosomes, such as deletions or translocations, are examined in chromosome spreads or by PCR. If no structural alterations exist, the presence of point mutations are ascertained. Mutations observed in some or all affected individuals, but not in normal individuals, indicates that the mutation may cause the disease. However, complete sequencing of the polypeptide and the corresponding gene from several normal individuals is
20 required to distinguish the mutation from a polymorphism. If a new polymorphism is identified, this polymorphic polypeptide can be used for further linkage analysis.

Furthermore, increased or decreased expression of the gene in affected individuals as compared to unaffected individuals can be assessed using the polynucleotides of the invention. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be
25 used as a diagnostic or prognostic marker. Diagnostic and prognostic methods, kits and reagents encompassed by the present invention are briefly described below and more thoroughly elsewhere herein (see e.g., the sections labeled "Antibodies", "Diagnostic Assays", and "Methods for Detecting Diseases").

Thus, the invention also provides a diagnostic method useful during diagnosis of a
30 disorder, involving measuring the expression level of polynucleotides of the present invention in cells or body fluid from an individual and comparing the measured gene expression level with a standard level of polynucleotide expression level, whereby an increase or decrease in the gene expression level compared to the standard is indicative of a disorder. Additional non-limiting examples of diagnostic methods encompassed by the present invention are more thoroughly
35 described elsewhere herein (see, e.g., Example 12).

In still another embodiment, the invention includes a kit for analyzing samples for the presence of proliferative and/or cancerous polynucleotides derived from a test subject. In a general

embodiment, the kit includes at least one polynucleotide probe containing a nucleotide sequence that will specifically hybridize with a polynucleotide of the invention and a suitable container. In a specific embodiment, the kit includes two polynucleotide probes defining an internal region of the polynucleotide of the invention, where each probe has one strand containing a 31' mer-end internal
5 to the region. In a further embodiment, the probes may be useful as primers for polymerase chain reaction amplification.

Where a diagnosis of a related disorder, including, for example, diagnosis of a tumor, has already been made according to conventional methods, the present invention is useful as a prognostic indicator, whereby patients exhibiting enhanced or depressed polynucleotide of the
10 invention expression will experience a worse clinical outcome relative to patients expressing the gene at a level nearer the standard level.

By "measuring the expression level of polynucleotides of the invention" is intended qualitatively or quantitatively measuring or estimating the level of the polypeptide of the invention or the level of the mRNA encoding the polypeptide of the invention in a first biological sample
15 either directly (e.g., by determining or estimating absolute protein level or mRNA level) or relatively (e.g., by comparing to the polypeptide level or mRNA level in a second biological sample). Preferably, the polypeptide level or mRNA level in the first biological sample is measured or estimated and compared to a standard polypeptide level or mRNA level, the standard
20 being taken from a second biological sample obtained from an individual not having the related disorder or being determined by averaging levels from a population of individuals not having a related disorder. As will be appreciated in the art, once a standard polypeptide level or mRNA level is known, it can be used repeatedly as a standard for comparison.

By "biological sample" is intended any biological sample obtained from an individual, body fluid, cell line, tissue culture, or other source which contains polypeptide of the present
25 invention or the corresponding mRNA. As indicated, biological samples include body fluids (such as semen, lymph, vaginal pool, sera, plasma, urine, synovial fluid and spinal fluid) which contain the polypeptide of the present invention, and tissue sources found to express the polypeptide of the present invention. Methods for obtaining tissue biopsies and body fluids from mammals are well known in the art. Where the biological sample is to include mRNA, a tissue biopsy is the
30 preferred source.

The method(s) provided above may preferably be applied in a diagnostic method and/or kits in which polynucleotides and/or polypeptides of the invention are attached to a solid support. In one exemplary method, the support may be a "gene chip" or a "biological chip" as described in US Patents 5,837,832, 5,874,219, and 5,856,174. Further, such a gene chip with polynucleotides
35 of the invention attached may be used to identify polymorphisms between the isolated polynucleotide sequences of the invention, with polynucleotides isolated from a test subject. The knowledge of such polymorphisms (i.e. their location, as well as, their existence) would be

beneficial in identifying disease loci for many disorders, such as for example, in neural disorders, immune system disorders, muscular disorders, reproductive disorders, gastrointestinal disorders, pulmonary disorders, digestive disorders, metabolic disorders, cardiovascular disorders, renal disorders, proliferative disorders, and/or cancerous diseases and conditions. Such a method is described in US Patents 5,858,659 and 5,856,104. The US Patents referenced *supra* are hereby
5 incorporated by reference in their entirety herein.

The present invention encompasses polynucleotides of the present invention that are chemically synthesized, or reproduced as peptide nucleic acids (PNA), or according to other methods known in the art. The use of PNAs would serve as the preferred form if the polynucleotides of the invention are incorporated onto a solid support, or gene chip. For the
10 purposes of the present invention, a peptide nucleic acid (PNA) is a polyamide type of DNA analog and the monomeric units for adenine, guanine, thymine and cytosine are available commercially (Perceptive Biosystems). Certain components of DNA, such as phosphorus, phosphorus oxides, or deoxyribose derivatives, are not present in PNAs. As disclosed by Nielsen
15 et al., Science 254, 1497 (1991); and Egholm et al., Nature 365, 666 (1993), PNAs bind specifically and tightly to complementary DNA strands and are not degraded by nucleases. In fact, PNA binds more strongly to DNA than DNA itself does. This is probably because there is no electrostatic repulsion between the two strands, and also the polyamide backbone is more flexible. Because of this, PNA/DNA duplexes bind under a wider range of stringency conditions than
20 DNA/DNA duplexes, making it easier to perform multiplex hybridization. Smaller probes can be used than with DNA due to the strong binding. In addition, it is more likely that single base mismatches can be determined with PNA/DNA hybridization because a single mismatch in a PNA/DNA 15-mer lowers the melting point ($T_{sub.m}$) by 8°-20° C, vs. 4°-16° C for the DNA/DNA 15-mer duplex. Also, the absence of charge groups in PNA means that hybridization
25 can be done at low ionic strengths and reduce possible interference by salt during the analysis.

The compounds of the present invention have uses which include, but are not limited to, detecting cancer in mammals. In particular the invention is useful during diagnosis of pathological cell proliferative neoplasias which include, but are not limited to: acute myelogenous leukemias including acute monocytic leukemia, acute myeloblastic leukemia, acute promyelocytic leukemia,
30 acute myelomonocytic leukemia, acute erythroleukemia, acute megakaryocytic leukemia, and acute undifferentiated leukemia, etc.; and chronic myelogenous leukemias including chronic myelomonocytic leukemia, chronic granulocytic leukemia, etc. Preferred mammals include monkeys, apes, cats, dogs, cows, pigs, horses, rabbits and humans. Particularly preferred are humans.

35 Pathological cell proliferative disorders are often associated with inappropriate activation of proto-oncogenes. (Germann, E. P. et al., "The Etiology of Acute Leukemia: Molecular Genetics and Viral Oncology," in Neoplastic Diseases of the Blood, Vol 1., Wiernik, P. H. et al. eds., 161-

182 (1985)). Neoplasias are now believed to result from the qualitative alteration of a normal cellular gene product, or from the quantitative modification of gene expression by insertion into the chromosome of a viral sequence, by chromosomal translocation of a gene to a more actively transcribed region, or by some other mechanism. (Germann et al., *supra*) It is likely that mutated
5 or altered expression of specific genes is involved in the pathogenesis of some leukemias, among other tissues and cell types. (Germann et al., *supra*) Indeed, the human counterparts of the oncogenes involved in some animal neoplasias have been amplified or translocated in some cases of human leukemia and carcinoma. (Germann et al., *supra*)

For example, c-myc expression is highly amplified in the non-lymphocytic leukemia cell
10 line HL-60. When HL-60 cells are chemically induced to stop proliferation, the level of c-myc is found to be downregulated. (International Publication Number WO 91/15580). However, it has been shown that exposure of HL-60 cells to a DNA construct that is complementary to the 5' end of c-myc or c-myb blocks translation of the corresponding mRNAs which downregulates
15 expression of the c-myc or c-myb proteins and causes arrest of cell proliferation and differentiation of the treated cells. (International Publication Number WO 91/15580; Wickstrom et al., Proc. Natl. Acad. Sci. 85:1028 (1988); Anfossi et al., Proc. Natl. Acad. Sci. 86:3379 (1989)). However, the skilled artisan would appreciate the present invention's usefulness is not be limited to treatment, prevention, and/or prognosis of proliferative disorders of cells and tissues of hematopoietic origin, in light of the numerous cells and cell types of varying origins which are
20 known to exhibit proliferative phenotypes.

In addition to the foregoing, a polynucleotide of the present invention can be used to control gene expression through triple helix formation or through antisense DNA or RNA. Antisense techniques are discussed, for example, in Okano, J. Neurochem. 56: 560 (1991); "Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL
25 (1988). Triple helix formation is discussed in, for instance Lee et al., Nucleic Acids Research 6: 3073 (1979); Cooney et al., Science 241: 456 (1988); and Dervan et al., Science 251: 1360 (1991). Both methods rely on binding of the polynucleotide to a complementary DNA or RNA. For these techniques, preferred polynucleotides are usually oligonucleotides 20 to 40 bases in length and complementary to either the region of the gene involved in transcription (triple helix - see Lee et
30 al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxy-nucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. The
35 oligonucleotide described above can also be delivered to cells such that the antisense RNA or DNA may be expressed *in vivo* to inhibit production of polypeptide of the present invention antigens. Both techniques are effective in model systems, and the information disclosed herein

can be used to design antisense or triple helix polynucleotides in an effort to treat disease, and in particular, for the treatment of proliferative diseases and/or conditions. Non-limiting antisense and triple helix methods encompassed by the present invention are more thoroughly described elsewhere herein (see, e.g., the section labeled "Antisense and Ribozyme (Antagonists)").

5 Polynucleotides of the present invention are also useful in gene therapy. One goal of gene therapy is to insert a normal gene into an organism having a defective gene, in an effort to correct the genetic defect. The polynucleotides disclosed in the present invention offer a means of targeting such genetic defects in a highly accurate manner. Another goal is to insert a new gene that was not present in the host genome, thereby producing a new trait in the host cell. Additional
10 non-limiting examples of gene therapy methods encompassed by the present invention are more thoroughly described elsewhere herein (see, e.g., the sections labeled "Gene Therapy Methods", and Examples 16, 17 and 18).

The polynucleotides are also useful for identifying individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment
15 length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identifying personnel. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The polynucleotides of the present invention can be used as additional DNA markers for
20 RFLP.

The polynucleotides of the present invention can also be used as an alternative to RFLP, by determining the actual base-by-base DNA sequence of selected portions of an individual's genome. These sequences can be used to prepare PCR primers for amplifying and isolating such selected DNA, which can then be sequenced. Using this technique, individuals can be identified
25 because each individual will have a unique set of DNA sequences. Once an unique ID database is established for an individual, positive identification of that individual, living or dead, can be made from extremely small tissue samples.

Forensic biology also benefits from using DNA-based identification techniques as disclosed herein. DNA sequences taken from very small biological samples such as tissues, e.g.,
30 hair or skin, or body fluids, e.g., blood, saliva, semen, synovial fluid, amniotic fluid, breast milk, lymph, pulmonary sputum or surfactant, urine, fecal matter, etc., can be amplified using PCR. In one prior art technique, gene sequences amplified from polymorphic loci, such as DQa class II HLA gene, are used in forensic biology to identify individuals. (Erich, H., PCR Technology, Freeman and Co. (1992)). Once these specific polymorphic loci are amplified, they are digested
35 with one or more restriction enzymes, yielding an identifying set of bands on a Southern blot probed with DNA corresponding to the DQa class II HLA gene. Similarly, polynucleotides of the present invention can be used as polymorphic markers for forensic purposes.

There is also a need for reagents capable of identifying the source of a particular tissue. Such need arises, for example, in forensics when presented with tissue of unknown origin. Appropriate reagents can comprise, for example, DNA probes or primers prepared from the sequences of the present invention, specific to tissues, including but not limited to those shown in
5 Table 1B. Panels of such reagents can identify tissue by species and/or by organ type. In a similar fashion, these reagents can be used to screen tissue cultures for contamination. Additional non-limiting examples of such uses are further described herein.

The polynucleotides of the present invention are also useful as hybridization probes for differential identification of the tissue(s) or cell type(s) present in a biological sample. Similarly,
10 polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of the tissue(s) (e.g., immunohistochemistry assays) or cell type(s) (e.g., immunocytochemistry assays). In addition, for a number of disorders of the above tissues or cells, significantly higher or lower levels of gene expression of the polynucleotides/polypeptides of the present invention may be detected in certain tissues (e.g.,
15 tissues expressing polypeptides and/or polynucleotides of the present invention, for example, those disclosed in Table 1B, and/or cancerous and/or wounded tissues) or bodily fluids (e.g., semen, lymph, vaginal pool, serum, plasma, urine, synovial fluid or spinal fluid) taken from an individual having such a disorder, relative to a "standard" gene expression level, i.e., the expression level in healthy tissue from an individual not having the disorder.

20 Thus, the invention provides a diagnostic method of a disorder, which involves: (a) assaying gene expression level in cells or body fluid of an individual; (b) comparing the gene expression level with a standard gene expression level, whereby an increase or decrease in the assayed gene expression level compared to the standard expression level is indicative of a disorder.

25 In the very least, the polynucleotides of the present invention can be used as molecular weight markers on Southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to "subtract-out" known sequences in the process of discovering novel polynucleotides, for selecting and making oligomers for attachment to a "gene chip" or other support, to raise anti-DNA antibodies using DNA immunization techniques, and as an antigen to
30 elicit an immune response.

Uses of the Polypeptides

Each of the polypeptides identified herein can be used in numerous ways. The following description should be considered exemplary and utilizes known techniques.

35 Polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of the tissue(s) (e.g.,

immunohistochemistry assays such as, for example, ABC immunoperoxidase (Hsu et al., J. Histochem. Cytochem. 29:577-580 (1981)) or cell type(s) (e.g., immunocytochemistry assays).

Antibodies can be used to assay levels of polypeptides encoded by polynucleotides of the invention in a biological sample using classical immunohistological methods known to those of skill in the art (e.g., see Jalkanen, et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, et al., J. Cell. Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine (^{131}I , ^{125}I , ^{123}I , ^{121}I), carbon (^{14}C), sulfur (^{35}S), tritium (^3H), indium ($^{115\text{m}}\text{In}$, $^{113\text{m}}\text{In}$, ^{112}In , ^{111}In), and technetium ($^{99\text{m}}\text{Tc}$, $^{99\text{m}}\text{Tc}$), thallium (^{201}Tl), gallium (^{68}Ga , ^{67}Ga), palladium (^{103}Pd), molybdenum (^{99}Mo), xenon (^{133}Xe), fluorine (^{18}F), ^{153}Sm , ^{177}Lu , ^{159}Gd , ^{149}Pm , ^{140}La , ^{175}Yb , ^{166}Ho , ^{90}Y , ^{47}Sc , ^{186}Re , ^{188}Re , ^{142}Pr , ^{105}Rh , ^{97}Ru ; luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

In addition to assaying levels of polypeptide of the present invention in a biological sample, proteins can also be detected *in vivo* by imaging. Antibody labels or markers for *in vivo* imaging of protein include those detectable by X-radiography, NMR or ESR. For X-radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of nutrients for the relevant hybridoma.

A protein-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example, ^{131}I , ^{112}In , $^{99\text{m}}\text{Tc}$, (^{131}I , ^{125}I , ^{123}I , ^{121}I), carbon (^{14}C), sulfur (^{35}S), tritium (^3H), indium ($^{115\text{m}}\text{In}$, $^{113\text{m}}\text{In}$, ^{112}In , ^{111}In), and technetium ($^{99\text{m}}\text{Tc}$, $^{99\text{m}}\text{Tc}$), thallium (^{201}Tl), gallium (^{68}Ga , ^{67}Ga), palladium (^{103}Pd), molybdenum (^{99}Mo), xenon (^{133}Xe), fluorine (^{18}F , ^{153}Sm , ^{177}Lu , ^{159}Gd , ^{149}Pm , ^{140}La , ^{175}Yb , ^{166}Ho , ^{90}Y , ^{47}Sc , ^{186}Re , ^{188}Re , ^{142}Pr , ^{105}Rh , ^{97}Ru), a radio-opaque substance, or a material detectable by nuclear magnetic resonance, is introduced (for example, parenterally, subcutaneously or intraperitoneally) into the mammal to be examined for immune system disorder. It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of $^{99\text{m}}\text{Tc}$. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which express the polypeptide encoded by a polynucleotide of the invention. *In vivo* tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments" (Chapter 13 in *Tumor Imaging: The Radiochemical Detection of Cancer*, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982)).

In one embodiment, the invention provides a method for the specific delivery of compositions of the invention to cells by administering polypeptides of the invention (e.g., polypeptides encoded by polynucleotides of the invention and/or antibodies) that are associated with heterologous polypeptides or nucleic acids. In one example, the invention provides a method
5 for delivering a therapeutic protein into the targeted cell. In another example, the invention provides a method for delivering a single stranded nucleic acid (e.g., antisense or ribozymes) or double stranded nucleic acid (e.g., DNA that can integrate into the cell's genome or replicate episomally and that can be transcribed) into the targeted cell.

In another embodiment, the invention provides a method for the specific destruction of
10 cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention in association with toxins or cytotoxic prodrugs.

By "toxin" is meant one or more compounds that bind and activate endogenous cytotoxic effector systems, radioisotopes, holotoxins, modified toxins, catalytic subunits of toxins, or any molecules or enzymes not normally present in or on the surface of a cell that under defined
15 conditions cause the cell's death. Toxins that may be used according to the methods of the invention include, but are not limited to, radioisotopes known in the art, compounds such as, for example, antibodies (or complement fixing containing portions thereof) that bind an inherent or induced endogenous cytotoxic effector system, thymidine kinase, endonuclease, RNase, alpha toxin, ricin, abrin, *Pseudomonas* exotoxin A, diphtheria toxin, saporin, momordin, gelonin,
20 pokeweed antiviral protein, alpha-sarcin and cholera toxin. "Toxin" also includes a cytostatic or cytotoxic agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example, ²¹³Bi, or other radioisotopes such as, for example, ¹⁰³Pd, ¹³³Xe, ¹³¹I, ⁶⁸Ge, ⁵⁷Co, ⁶⁵Zn, ⁸⁵Sr, ³²P, ³⁵S, ⁹⁰Y, ¹⁵³Sm, ¹⁵³Gd, ¹⁶⁹Yb, ⁵¹Cr, ⁵⁴Mn, ⁷⁵Se, ¹¹³Sn, ⁹⁰Yttrium, ¹¹⁷Tin, ¹⁸⁶Rhenium, ¹⁶⁶Holmium, and ¹⁸⁸Rhenium; luminescent labels, such as luminol; and fluorescent labels, such as
25 fluorescein and rhodamine, and biotin. In a specific embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention or antibodies of the invention in association with the radioisotope ⁹⁰Y. In another specific embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention or
30 antibodies of the invention in association with the radioisotope ¹¹¹In. In a further specific embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention or antibodies of the invention in association with the radioisotope ¹³¹I.

Techniques known in the art may be applied to label polypeptides of the invention
35 (including antibodies). Such techniques include, but are not limited to, the use of bifunctional conjugating agents (see e.g., U.S. Patent Nos. 5,756,065; 5,714,631; 5,696,239; 5,652,361;

5,505,931; 5,489,425; 5,435,990; 5,428,139; 5,342,604; 5,274,119; 4,994,560; and 5,808,003; the contents of each of which are hereby incorporated by reference in its entirety).

Thus, the invention provides a diagnostic method of a disorder, which involves (a) assaying the expression level of a polypeptide of the present invention in cells or body fluid of an individual; and (b) comparing the assayed polypeptide expression level with a standard polypeptide expression level, whereby an increase or decrease in the assayed polypeptide expression level compared to the standard expression level is indicative of a disorder. With respect to cancer, the presence of a relatively high amount of transcript in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

Moreover, polypeptides of the present invention can be used to treat or prevent diseases or conditions such as, for example, neural disorders, immune system disorders, muscular disorders, reproductive disorders, gastrointestinal disorders, pulmonary disorders, cardiovascular disorders, renal disorders, proliferative disorders, and/or cancerous diseases and conditions. For example, patients can be administered a polypeptide of the present invention in an effort to replace absent or decreased levels of the polypeptide (e.g., insulin), to supplement absent or decreased levels of a different polypeptide (e.g., hemoglobin S for hemoglobin B, SOD, catalase, DNA repair proteins), to inhibit the activity of a polypeptide (e.g., an oncogene or tumor suppressor), to activate the activity of a polypeptide (e.g., by binding to a receptor), to reduce the activity of a membrane bound receptor by competing with it for free ligand (e.g., soluble TNF receptors used in reducing inflammation), or to bring about a desired response (e.g., blood vessel growth inhibition, enhancement of the immune response to proliferative cells or tissues).

Similarly, antibodies directed to a polypeptide of the present invention can also be used to treat disease (as described *supra*, and elsewhere herein). For example, administration of an antibody directed to a polypeptide of the present invention can bind, and/or neutralize the polypeptide, and/or reduce overproduction of the polypeptide. Similarly, administration of an antibody can activate the polypeptide, such as by binding to a polypeptide bound to a membrane (receptor).

At the very least, the polypeptides of the present invention can be used as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods well known to those of skill in the art. Polypeptides can also be used to raise antibodies, which in turn are used to measure protein expression from a recombinant cell, as a way of assessing transformation of the host cell. Moreover, the polypeptides of the present invention can be used to test the biological activities described herein.

Diagnostic Assays

The compounds of the present invention are useful for diagnosis, treatment, prevention and/or prognosis of various disorders in mammals, preferably humans. Such disorders include, but are not limited to, those related to biological activities described in Table 1D and, also as described
5 herein under the section heading "Biological Activities".

For a number of disorders, substantially altered (increased or decreased) levels of gene expression can be detected in tissues, cells or bodily fluids (e.g., sera, plasma, urine, semen, synovial fluid or spinal fluid) taken from an individual having such a disorder, relative to a
10 "standard" gene expression level, that is, the expression level in tissues or bodily fluids from an individual not having the disorder. Thus, the invention provides a diagnostic method useful during diagnosis of a disorder, which involves measuring the expression level of the gene encoding the polypeptide in tissues, cells or body fluid from an individual and comparing the measured gene expression level with a standard gene expression level, whereby an increase or decrease in the
15 gene expression level(s) compared to the standard is indicative of a disorder. These diagnostic assays may be performed *in vivo* or *in vitro*, such as, for example, on blood samples, biopsy tissue or autopsy tissue.

The present invention is also useful as a prognostic indicator, whereby patients exhibiting enhanced or depressed gene expression will experience a worse clinical outcome relative to
20 patients expressing the gene at a level nearer the standard level.

In certain embodiments, a polypeptide of the invention, or polynucleotides, antibodies, agonists, or antagonists corresponding to that polypeptide, may be used to diagnose and/or prognosticate diseases and/or disorders associated with the tissue(s) in which the polypeptide of the invention is expressed, including one, two, three, four, five, or more tissues disclosed in Table
25 1B.2, column 5 (Tissue Distribution Library Code).

By "assaying the expression level of the gene encoding the polypeptide" is intended qualitatively or quantitatively measuring or estimating the level of the polypeptide of the invention or the level of the mRNA encoding the polypeptide of the invention in a first biological sample either directly (e.g., by determining or estimating absolute protein level or mRNA level) or
30 relatively (e.g., by comparing to the polypeptide level or mRNA level in a second biological sample). Preferably, the polypeptide expression level or mRNA level in the first biological sample is measured or estimated and compared to a standard polypeptide level or mRNA level, the standard being taken from a second biological sample obtained from an individual not having the disorder or being determined by averaging levels from a population of individuals not having the
35 disorder. As will be appreciated in the art, once a standard polypeptide level or mRNA level is known, it can be used repeatedly as a standard for comparison.

By "biological sample" is intended any biological sample obtained from an individual, cell

line, tissue culture, or other source containing polypeptides of the invention (including portions thereof) or mRNA. As indicated, biological samples include body fluids (such as sera, plasma, urine, synovial fluid and spinal fluid) and tissue sources found to express the full length or fragments thereof of a polypeptide or mRNA. Methods for obtaining tissue biopsies and body fluids from mammals are well known in the art. Where the biological sample is to include mRNA, a tissue biopsy is the preferred source.

Total cellular RNA can be isolated from a biological sample using any suitable technique such as the single-step guanidinium-thiocyanate-phenol-chloroform method described in Chomczynski and Sacchi, *Anal. Biochem.* 162:156-159 (1987). Levels of mRNA encoding the polypeptides of the invention are then assayed using any appropriate method. These include Northern blot analysis, S1 nuclease mapping, the polymerase chain reaction (PCR), reverse transcription in combination with the polymerase chain reaction (RT-PCR), and reverse transcription in combination with the ligase chain reaction (RT-LCR).

The present invention also relates to diagnostic assays such as quantitative and diagnostic assays for detecting levels of polypeptides of the invention, in a biological sample (e.g., cells and tissues), including determination of normal and abnormal levels of polypeptides. Thus, for instance, a diagnostic assay in accordance with the invention for detecting over-expression of polypeptides of the invention compared to normal control tissue samples may be used to detect the presence of tumors. Assay techniques that can be used to determine levels of a polypeptide, such as a polypeptide of the present invention in a sample derived from a host are well-known to those of skill in the art. Such assay methods include radioimmunoassays, competitive-binding assays, Western Blot analysis and ELISA assays. Assaying polypeptide levels in a biological sample can occur using any art-known method.

Assaying polypeptide levels in a biological sample can occur using antibody-based techniques. For example, polypeptide expression in tissues can be studied with classical immunohistological methods (Jalkanen et al., *J. Cell. Biol.* 101:976-985 (1985); Jalkanen, M., et al., *J. Cell. Biol.* 105:3087-3096 (1987)). Other antibody-based methods useful for detecting polypeptide gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase, and radioisotopes, such as iodine (^{125}I , ^{121}I), carbon (^{14}C), sulfur (^{35}S), tritium (^3H), indium (^{112}In), and technetium ($^{99\text{m}}\text{Tc}$), and fluorescent labels, such as fluorescein and rhodamine, and biotin.

The tissue or cell type to be analyzed will generally include those which are known, or suspected, to express the gene of interest (such as, for example, cancer). The protein isolation methods employed herein may, for example, be such as those described in Harlow and Lane (Harlow, E. and Lane, D., 1988, "Antibodies: A Laboratory Manual", Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York), which is incorporated herein by reference in its

entirety. The isolated cells can be derived from cell culture or from a patient. The analysis of cells taken from culture may be a necessary step in the assessment of cells that could be used as part of a cell-based gene therapy technique or, alternatively, to test the effect of compounds on the expression of the gene.

5 For example, antibodies, or fragments of antibodies, such as those described herein, may be used to quantitatively or qualitatively detect the presence of gene products or conserved variants or peptide fragments thereof. This can be accomplished, for example, by immunofluorescence techniques employing a fluorescently labeled antibody coupled with light microscopic, flow cytometric, or fluorimetric detection.

10 In a preferred embodiment, antibodies, or fragments of antibodies directed to any one or all of the predicted epitope domains of the polypeptides of the invention (shown in column 7 of Table 1B.1) may be used to quantitatively or qualitatively detect the presence of gene products or conserved variants or peptide fragments thereof. This can be accomplished, for example, by immunofluorescence techniques employing a fluorescently labeled antibody coupled with light
15 microscopic, flow cytometric, or fluorimetric detection.

In an additional preferred embodiment, antibodies, or fragments of antibodies directed to a conformational epitope of a polypeptide of the invention may be used to quantitatively or qualitatively detect the presence of gene products or conserved variants or peptide fragments thereof. This can be accomplished, for example, by immunofluorescence techniques employing a
20 fluorescently labeled antibody coupled with light microscopic, flow cytometric, or fluorimetric detection.

The antibodies (or fragments thereof), and/or polypeptides of the present invention may, additionally, be employed histologically, as in immunofluorescence, immunoelectron microscopy or non-immunological assays, for in situ detection of gene products or conserved variants or
25 peptide fragments thereof. In situ detection may be accomplished by removing a histological specimen from a patient, and applying thereto a labeled antibody or polypeptide of the present invention. The antibody (or fragment thereof) or polypeptide is preferably applied by overlaying the labeled antibody (or fragment) onto a biological sample. Through the use of such a procedure, it is possible to determine not only the presence of the gene product, or conserved variants or
30 peptide fragments, or polypeptide binding, but also its distribution in the examined tissue. Using the present invention, those of ordinary skill will readily perceive that any of a wide variety of histological methods (such as staining procedures) can be modified in order to achieve such in situ detection.

Immunoassays and non-immunoassays for gene products or conserved variants or peptide
35 fragments thereof will typically comprise incubating a sample, such as a biological fluid, a tissue extract, freshly harvested cells, or lysates of cells which have been incubated in cell culture, in the presence of a detectably labeled antibody capable of binding gene products or conserved variants

or peptide fragments thereof, and detecting the bound antibody by any of a number of techniques well-known in the art.

The biological sample may be brought in contact with and immobilized onto a solid phase support or carrier such as nitrocellulose, or other solid support which is capable of immobilizing cells, cell particles or soluble proteins. The support may then be washed with suitable buffers followed by treatment with the detectably labeled antibody or detectable polypeptide of the invention. The solid phase support may then be washed with the buffer a second time to remove unbound antibody or polypeptide. Optionally the antibody is subsequently labeled. The amount of bound label on solid support may then be detected by conventional means.

By "solid phase support or carrier" is intended any support capable of binding an antigen or an antibody. Well-known supports or carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, gabbros, and magnetite. The nature of the carrier can be either soluble to some extent or insoluble for the purposes of the present invention. The support material may have virtually any possible structural configuration so long as the coupled molecule is capable of binding to an antigen or antibody. Thus, the support configuration may be spherical, as in a bead, or cylindrical, as in the inside surface of a test tube, or the external surface of a rod. Alternatively, the surface may be flat such as a sheet, test strip, etc. Preferred supports include polystyrene beads. Those skilled in the art will know many other suitable carriers for binding antibody or antigen, or will be able to ascertain the same by use of routine experimentation.

The binding activity of a given lot of antibody or antigen polypeptide may be determined according to well known methods. Those skilled in the art will be able to determine operative and optimal assay conditions for each determination by employing routine experimentation.

In addition to assaying polypeptide levels or polynucleotide levels in a biological sample obtained from an individual, polypeptide or polynucleotide can also be detected *in vivo* by imaging. For example, in one embodiment of the invention, polypeptides and/or antibodies of the invention are used to image diseased cells, such as neoplasms. In another embodiment, polynucleotides of the invention (e.g., polynucleotides complementary to all or a portion of an mRNA) and/or antibodies (e.g., antibodies directed to any one or a combination of the epitopes of a polypeptide of the invention, antibodies directed to a conformational epitope of a polypeptide of the invention, or antibodies directed to the full length polypeptide expressed on the cell surface of a mammalian cell) are used to image diseased or neoplastic cells.

Antibody labels or markers for *in vivo* imaging of polypeptides of the invention include those detectable by X-radiography, NMR, MRI, CAT-scans or ESR. For X-radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of

nutrients for the relevant hybridoma. Where *in vivo* imaging is used to detect enhanced levels of polypeptides for diagnosis in humans, it may be preferable to use human antibodies or "humanized" chimeric monoclonal antibodies. Such antibodies can be produced using techniques described herein or otherwise known in the art. For example methods for producing chimeric antibodies are known in the art. See, for review, Morrison, *Science* 229:1202 (1985); Oi et al., *BioTechniques* 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496; Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., WO 8702671; Boulianne et al., *Nature* 312:643 (1984); Neuberger et al., *Nature* 314:268 (1985).

Additionally, any polypeptides of the invention whose presence can be detected, can be administered. For example, polypeptides of the invention labeled with a radio-opaque or other appropriate compound can be administered and visualized *in vivo*, as discussed, above for labeled antibodies. Further, such polypeptides can be utilized for *in vitro* diagnostic procedures.

A polypeptide-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example, ^{131}I , ^{112}In , $^{99\text{m}}\text{Tc}$), a radio-opaque substance, or a material detectable by nuclear magnetic resonance, is introduced (for example, parenterally, subcutaneously or intraperitoneally) into the mammal to be examined for a disorder. It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of $^{99\text{m}}\text{Tc}$. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain the antigenic protein. *In vivo* tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments" (Chapter 13 in *Tumor Imaging: The Radiochemical Detection of Cancer*, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982)).

With respect to antibodies, one of the ways in which an antibody of the present invention can be detectably labeled is by linking the same to a reporter enzyme and using the linked product in an enzyme immunoassay (EIA) (Voller, A., "The Enzyme Linked Immunosorbent Assay (ELISA)", 1978, Diagnostic Horizons 2:1-7, Microbiological Associates Quarterly Publication, Walkersville, MD); Voller et al., *J. Clin. Pathol.* 31:507-520 (1978); Butler, J.E., *Meth. Enzymol.* 73:482-523 (1981); Maggio, E. (ed.), 1980, Enzyme Immunoassay, CRC Press, Boca Raton, FL.; Ishikawa, E. et al., (eds.), 1981, Enzyme Immunoassay, Kigaku Shoin, Tokyo). The reporter enzyme which is bound to the antibody will react with an appropriate substrate, preferably a chromogenic substrate, in such a manner as to produce a chemical moiety which can be detected, for example, by spectrophotometric, fluorimetric or by visual means. Reporter enzymes which can be used to detectably label the antibody include, but are not limited to, malate dehydrogenase, staphylococcal nuclease, delta-5-steroid isomerase, yeast alcohol dehydrogenase, alpha-glycerophosphate, dehydrogenase, triose phosphate isomerase, horseradish peroxidase, alkaline

phosphatase, asparaginase, glucose oxidase, beta-galactosidase, ribonuclease, urease, catalase, glucose-6-phosphate dehydrogenase, glucoamylase and acetylcholinesterase. Additionally, the detection can be accomplished by colorimetric methods which employ a chromogenic substrate for the reporter enzyme. Detection may also be accomplished by visual comparison of the extent of enzymatic reaction of a substrate in comparison with similarly prepared standards.

5 Detection may also be accomplished using any of a variety of other immunoassays. For example, by radioactively labeling the antibodies or antibody fragments, it is possible to detect polypeptides through the use of a radioimmunoassay (RIA) (see, for example, Weintraub, B., Principles of Radioimmunoassays, Seventh Training Course on Radioligand Assay Techniques, 10 The Endocrine Society, March, 1986, which is incorporated by reference herein). The radioactive isotope can be detected by means including, but not limited to, a gamma counter, a scintillation counter, or autoradiography.

It is also possible to label the antibody with a fluorescent compound. When the fluorescently labeled antibody is exposed to light of the proper wave length, its presence can then be detected due to fluorescence. Among the most commonly used fluorescent labeling compounds are fluorescein isothiocyanate, rhodamine, phycoerythrin, phycocyanin, allophycocyanin, ophthaldehyde and fluorescamine.

15 The antibody can also be detectably labeled using fluorescence emitting metals such as ¹⁵²Eu, or others of the lanthanide series. These metals can be attached to the antibody using such metal chelating groups as diethylenetriaminepentacetic acid (DTPA) or ethylenediaminetetraacetic acid (EDTA).

The antibody also can be detectably labeled by coupling it to a chemiluminescent compound. The presence of the chemiluminescent-tagged antibody is then determined by detecting the presence of luminescence that arises during the course of a chemical reaction. 25 Examples of particularly useful chemiluminescent labeling compounds are luminol, isoluminol, theromatic acridinium ester, imidazole, acridinium salt and oxalate ester.

Likewise, a bioluminescent compound may be used to label the antibody of the present invention. Bioluminescence is a type of chemiluminescence found in biological systems in, which a catalytic protein increases the efficiency of the chemiluminescent reaction. The presence of a bioluminescent protein is determined by detecting the presence of luminescence. Important 30 bioluminescent compounds for purposes of labeling are luciferin, luciferase and aequorin.

Methods for Detecting Diseases

In general, a disease may be detected in a patient based on the presence of one or more proteins of the invention and/or polynucleotides encoding such proteins in a biological sample (for 35 example, blood, sera, urine, and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a disease or disorder,

including cancer and/or as described elsewhere herein. In addition, such proteins may be useful for the detection of other diseases and cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding polypeptides of the invention, which is also indicative of the presence or absence of a disease or disorder, including cancer. In general, polypeptides of the invention should be present at a level that is at least three fold higher in diseased tissue than in normal tissue.

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, *supra*. In general, the presence or absence of a disease in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of a binding agent(s) immobilized on a solid support to bind to and remove the polypeptide of the invention from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include polypeptides of the invention and portions thereof, or antibodies, to which the binding agent binds, as described above.

The solid support may be any material known to those of skill in the art to which polypeptides of the invention may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a

microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for the suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 ug, and preferably about 100 ng to about 1 ug, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

Gene Therapy Methods

Also encompassed by the invention are gene therapy methods for treating or preventing disorders, diseases and conditions. The gene therapy methods relate to the introduction of nucleic acid (DNA, RNA and antisense DNA or RNA) sequences into an animal to achieve expression of the polypeptide of the present invention. This method requires a polynucleotide which codes for a polypeptide of the present invention operatively linked to a promoter and any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques are known in the art, see, for example, WO90/11092, which is herein incorporated by reference.

Thus, for example, cells from a patient may be engineered with a polynucleotide (DNA or RNA) comprising a promoter operably linked to a polynucleotide of the present invention ex vivo, with the engineered cells then being provided to a patient to be treated with the polypeptide of the present invention. Such methods are well-known in the art. For example, see Belldgrun, A., et al., J. Natl. Cancer Inst. 85: 207-216 (1993); Ferrantini, M. et al., Cancer Research 53: 1107-1112 (1993); Ferrantini, M. et al., J. Immunology 153: 4604-4615 (1994); Kaido, T., et al., Int. J. Cancer 60: 221-229 (1995); Ogura, H., et al., Cancer Research 50: 5102-5106 (1990); Santodonato, L., et al., Human Gene Therapy 7:1-10 (1996); Santodonato, L., et al., Gene Therapy 4:1246-1255 (1997); and Zhang, J.-F. et al., Cancer Gene Therapy 3: 31-38 (1996)), which are herein incorporated by reference. In one embodiment, the cells which are engineered are arterial cells. The arterial cells may be reintroduced into the patient through direct injection to the artery, the tissues surrounding the artery, or through catheter injection.

As discussed in more detail below, the polynucleotide constructs can be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, and the like). The polynucleotide constructs may be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

5 In one embodiment, the polynucleotide of the present invention is delivered as a naked polynucleotide. The term "naked" polynucleotide, DNA or RNA refers to sequences that are free from any delivery vehicle that acts to assist, promote or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotide of the present invention can also be delivered in liposome
10 formulations and lipofectin formulations and the like can be prepared by methods well known to those skilled in the art. Such methods are described, for example, in U.S. Patent Nos. 5,593,972, 5,589,466, and 5,580,859, which are herein incorporated by reference.

The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow
15 for replication. Appropriate vectors include pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; pSVK3, pBPV, pMSG and pSVL available from Pharmacia; and pEF1/V5, pcDNA3.1, and pRc/CMV2 available from Invitrogen. Other suitable vectors will be readily apparent to the skilled artisan.

Any strong promoter known to those skilled in the art can be used for driving the
20 expression of the polynucleotide sequence. Suitable promoters include adenoviral promoters, such as the adenoviral major late promoter; or heterologous promoters, such as the cytomegalovirus (CMV) promoter; the respiratory syncytial virus (RSV) promoter; inducible promoters, such as the MMT promoter, the metallothionein promoter; heat shock promoters; the albumin promoter; the ApoAI promoter; human globin promoters; viral thymidine kinase promoters, such as the Herpes
25 Simplex thymidine kinase promoter; retroviral LTRs; the b-actin promoter; and human growth hormone promoters. The promoter also may be the native promoter for the polynucleotide of the present invention.

Unlike other gene therapy techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells.
30 Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus,
35 rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular, fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same

matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. *In vivo* muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked nucleic acid sequence injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 mg/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration.

The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked DNA constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The naked polynucleotides are delivered by any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical administration, catheter infusion, and so-called "gene guns". These delivery methods are known in the art.

The constructs may also be delivered with delivery vehicles such as viral sequences, viral particles, liposome formulations, lipofectin, precipitating agents, etc. Such methods of delivery are known in the art.

In certain embodiments, the polynucleotide constructs are complexed in a liposome preparation. Liposomal preparations for use in the instant invention include cationic (positively charged), anionic (negatively charged) and neutral preparations. However, cationic liposomes are particularly preferred because a tight charge complex can be formed between the cationic liposome and the polyanionic nucleic acid. Cationic liposomes have been shown to mediate intracellular delivery of plasmid DNA (Felgner et al., Proc. Natl. Acad. Sci. USA (1987) 84:7413-7416, which is herein incorporated by reference); mRNA (Malone et al., Proc. Natl. Acad. Sci. USA (1989) 86:6077-6081, which is herein incorporated by reference); and purified transcription factors (Debs et al., J. Biol. Chem. (1990) 265:10189-10192, which is herein incorporated by reference), in functional form.

Cationic liposomes are readily available. For example, N[1-2,3-dioleoyloxy)propyl]-N,N,N-triethylammonium (DOTMA) liposomes are particularly useful and are available under the trademark Lipofectin, from GIBCO BRL, Grand Island, N.Y. (See, also, Felgner et al., Proc. Natl Acad. Sci. USA (1987) 84:7413-7416, which is herein
5 incorporated by reference). Other commercially available liposomes include transfectace (DDAB/DOPE) and DOTAP/DOPE (Boehringer).

Other cationic liposomes can be prepared from readily available materials using techniques well known in the art. See, e.g. PCT Publication No. WO 90/11092 (which is herein incorporated by reference) for a description of the synthesis of DOTAP (1,2-bis(oleoyloxy)-3-
10 (trimethylammonio)propane) liposomes. Preparation of DOTMA liposomes is explained in the literature, see, e.g., P. Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417, which is herein incorporated by reference. Similar methods can be used to prepare liposomes from other cationic lipid materials.

Similarly, anionic and neutral liposomes are readily available, such as from Avanti Polar
15 Lipids (Birmingham, Ala.), or can be easily prepared using readily available materials. Such materials include phosphatidyl, choline, cholesterol, phosphatidyl ethanolamine, dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), dioleoylphosphatidyl ethanolamine (DOPE), among others. These materials can also be mixed with the DOTMA and DOTAP starting materials in appropriate ratios. Methods for making liposomes
20 using these materials are well known in the art.

For example, commercially dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), and dioleoylphosphatidyl ethanolamine (DOPE) can be used in various combinations to make conventional liposomes, with or without the addition of cholesterol. Thus, for example, DOPG/DOPC vesicles can be prepared by drying 50 mg each of DOPG and DOPC
25 under a stream of nitrogen gas into a sonication vial. The sample is placed under a vacuum pump overnight and is hydrated the following day with deionized water. The sample is then sonicated for 2 hours in a capped vial, using a Heat Systems model 350 sonicator equipped with an inverted cup (bath type) probe at the maximum setting while the bath is circulated at 15EC. Alternatively, negatively charged vesicles can be prepared without sonication to produce multilamellar vesicles
30 or by extrusion through nucleopore membranes to produce unilamellar vesicles of discrete size. Other methods are known and available to those of skill in the art.

The liposomes can comprise multilamellar vesicles (MLVs), small unilamellar vesicles (SUVs), or large unilamellar vesicles (LUVs), with SUVs being preferred. The various liposome-nucleic acid complexes are prepared using methods well known in the art. See, e.g.,
35 Straubinger et al., Methods of Immunology (1983), 101:512-527, which is herein incorporated by reference. For example, MLVs containing nucleic acid can be prepared by depositing a thin film of phospholipid on the walls of a glass tube and subsequently hydrating with a solution of the

material to be encapsulated. SUVs are prepared by extended sonication of MLVs to produce a homogeneous population of unilamellar liposomes. The material to be entrapped is added to a suspension of preformed MLVs and then sonicated. When using liposomes containing cationic lipids, the dried lipid film is resuspended in an appropriate solution such as sterile water or an isotonic buffer solution such as 10 mM Tris/NaCl, sonicated, and then the preformed liposomes are mixed directly with the DNA. The liposome and DNA form a very stable complex due to binding of the positively charged liposomes to the cationic DNA. SUVs find use with small nucleic acid fragments. LUVs are prepared by a number of methods, well known in the art. Commonly used methods include Ca^{2+} -EDTA chelation (Papahadjopoulos et al., Biochim. Biophys. Acta (1975) 394:483; Wilson et al., Cell 17:77 (1979)); ether injection (Deamer, D. and Bangham, A., Biochim. Biophys. Acta 443:629 (1976); Ostro et al., Biochem. Biophys. Res. Commun. 76:836 (1977); Fraley et al., Proc. Natl. Acad. Sci. USA 76:3348 (1979)); detergent dialysis (Enoch, H. and Strittmatter, P., Proc. Natl. Acad. Sci. USA 76:145 (1979)); and reverse-phase evaporation (REV) (Fraley et al., J. Biol. Chem. 255:10431 (1980); Szoka, F. and Papahadjopoulos, D., Proc. Natl. Acad. Sci. USA 75:145 (1978); Schaefer-Ridder et al., Science 215:166 (1982)), which are herein incorporated by reference.

Generally, the ratio of DNA to liposomes will be from about 10:1 to about 1:10. Preferably, the ratio will be from about 5:1 to about 1:5. More preferably, the ratio will be about 3:1 to about 1:3. Still more preferably, the ratio will be about 1:1.

U.S. Patent No. 5,676,954 (which is herein incorporated by reference) reports on the injection of genetic material, complexed with cationic liposomes carriers, into mice. U.S. Patent Nos. 4,897,355, 4,946,787, 5,049,386, 5,459,127, 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication no. WO 94/9469 (which are herein incorporated by reference) provide cationic lipids for use in transfecting DNA into cells and mammals. U.S. Patent Nos. 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication no. WO 94/9469 provide methods for delivering DNA-cationic lipid complexes to mammals.

In certain embodiments, cells are engineered, *ex vivo* or *in vivo*, using a retroviral particle containing RNA which comprises a sequence encoding a polypeptide of the present invention. Retroviruses from which the retroviral plasmid vectors may be derived include, but are not limited to, Moloney Murine Leukemia Virus, spleen necrosis virus, Rous sarcoma Virus, Harvey Sarcoma Virus, avian leukosis virus, gibbon ape leukemia virus, human immunodeficiency virus, Myeloproliferative Sarcoma Virus, and mammary tumor virus.

The retroviral plasmid vector is employed to transduce packaging cell lines to form producer cell lines. Examples of packaging cells which may be transfected include, but are not limited to, the PE501, PA317, R-2, R-AM, PA12, T19-14X, VT-19-17-H2, RCRE, RCRIP, GP+E-86, GP+envAm12, and DAN cell lines as described in Miller, Human Gene Therapy 1:5-14 (1990), which is incorporated herein by reference in its entirety. The vector may transduce the

packaging cells through any means known in the art. Such means include, but are not limited to, electroporation, the use of liposomes, and CaPO_4 precipitation. In one alternative, the retroviral plasmid vector may be encapsulated into a liposome, or coupled to a lipid, and then administered to a host.

5 The producer cell line generates infectious retroviral vector particles which include polynucleotide encoding a polypeptide of the present invention. Such retroviral vector particles then may be employed, to transduce eukaryotic cells, either *in vitro* or *in vivo*. The transduced eukaryotic cells will express a polypeptide of the present invention.

10 In certain other embodiments, cells are engineered, *ex vivo* or *in vivo*, with polynucleotide contained in an adenovirus vector. Adenovirus can be manipulated such that it encodes and expresses a polypeptide of the present invention, and at the same time is inactivated in terms of its ability to replicate in a normal lytic viral life cycle. Adenovirus expression is achieved without integration of the viral DNA into the host cell chromosome, thereby alleviating concerns about insertional mutagenesis. Furthermore, adenoviruses have been used as live enteric vaccines for
15 many years with an excellent safety profile (Schwartz et al. *Am. Rev. Respir. Dis.* 109:233-238 (1974)). Finally, adenovirus mediated gene transfer has been demonstrated in a number of instances including transfer of alpha-1-antitrypsin and CFTR to the lungs of cotton rats (Rosenfeld, M. A. et al. (1991) *Science* 252:431-434; Rosenfeld et al., (1992) *Cell* 68:143-155). Furthermore, extensive studies to attempt to establish adenovirus as a causative agent in human
20 cancer were uniformly negative (Green, M. et al. (1979) *Proc. Natl. Acad. Sci. USA* 76:6606).

Suitable adenoviral vectors useful in the present invention are described, for example, in Kozarsky and Wilson, *Curr. Opin. Genet. Devel.* 3:499-503 (1993); Rosenfeld et al., *Cell* 68:143-155 (1992); Engelhardt et al., *Human Genet. Ther.* 4:759-769 (1993); Yang et al., *Nature Genet.* 7:362-369 (1994); Wilson et al., *Nature* 365:691-692 (1993); and U.S. Patent No. 5,652,224,
25 which are herein incorporated by reference. For example, the adenovirus vector Ad2 is useful and can be grown in human 293 cells. These cells contain the E1 region of adenovirus and constitutively express E1a and E1b, which complement the defective adenoviruses by providing the products of the genes deleted from the vector. In addition to Ad2, other varieties of adenovirus (e.g., Ad3, Ad5, and Ad7) are also useful in the present invention.

30 Preferably, the adenoviruses used in the present invention are replication deficient. Replication deficient adenoviruses require the aid of a helper virus and/or packaging cell line to form infectious particles. The resulting virus is capable of infecting cells and can express a polynucleotide of interest which is operably linked to a promoter, but cannot replicate in most cells. Replication deficient adenoviruses may be deleted in one or more of all or a portion of the
35 following genes: E1a, E1b, E3, E4, E2a, or L1 through L5.

In certain other embodiments, the cells are engineered, *ex vivo* or *in vivo*, using an adeno-associated virus (AAV). AAVs are naturally occurring defective viruses that require helper

viruses to produce infectious particles (Muzyczka, N., Curr. Topics in Microbiol. Immunol. 158:97 (1992)). It is also one of the few viruses that may integrate its DNA into non-dividing cells. Vectors containing as little as 300 base pairs of AAV can be packaged and can integrate, but space for exogenous DNA is limited to about 4.5 kb. Methods for producing and using such AAVs are known in the art. See, for example, U.S. Patent Nos. 5,139,941, 5,173,414, 5,354,678, 5,436,146, 5,474,935, 5,478,745, and 5,589,377.

For example, an appropriate AAV vector for use in the present invention will include all the sequences necessary for DNA replication, encapsidation, and host-cell integration. The polynucleotide construct is inserted into the AAV vector using standard cloning methods, such as those found in Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press (1989). The recombinant AAV vector is then transfected into packaging cells which are infected with a helper virus, using any standard technique, including lipofection, electroporation, calcium phosphate precipitation, etc. Appropriate helper viruses include adenoviruses, cytomegaloviruses, vaccinia viruses, or herpes viruses. Once the packaging cells are transfected and infected, they will produce infectious AAV viral particles which contain the polynucleotide construct. These viral particles are then used to transduce eukaryotic cells, either *ex vivo* or *in vivo*. The transduced cells will contain the polynucleotide construct integrated into its genome, and will express a polypeptide of the invention.

Another method of gene therapy involves operably associating heterologous control regions and endogenous polynucleotide sequences (e.g. encoding a polypeptide of the present invention) via homologous recombination (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989), which are herein incorporated by reference. This method involves the activation of a gene which is present in the target cells, but which is not normally expressed in the cells, or is expressed at a lower level than desired.

Polynucleotide constructs are made, using standard techniques known in the art, which contain the promoter with targeting sequences flanking the promoter. Suitable promoters are described herein. The targeting sequence is sufficiently complementary to an endogenous sequence to permit homologous recombination of the promoter-targeting sequence with the endogenous sequence. The targeting sequence will be sufficiently near the 5' end of the desired endogenous polynucleotide sequence so the promoter will be operably linked to the endogenous sequence upon homologous recombination.

The promoter and the targeting sequences can be amplified using PCR. Preferably, the amplified promoter contains distinct restriction enzyme sites on the 5' and 3' ends. Preferably, the 3' end of the first targeting sequence contains the same restriction enzyme site as the 5' end of the

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amplified promoter and the 5' end of the second targeting sequence contains the same restriction site as the 3' end of the amplified promoter. The amplified promoter and targeting sequences are digested and ligated together.

5 The promoter-targeting sequence construct is delivered to the cells, either as naked polynucleotide, or in conjunction with transfection-facilitating agents, such as liposomes, viral sequences, viral particles, whole viruses, lipofection, precipitating agents, etc., described in more detail above. The P promoter-targeting sequence can be delivered by any method, included direct needle injection, intravenous injection, topical administration, catheter infusion, particle accelerators, etc. The methods are described in more detail below.

10 The promoter-targeting sequence construct is taken up by cells. Homologous recombination between the construct and the endogenous sequence takes place, such that an endogenous sequence is placed under the control of the promoter. The promoter then drives the expression of the endogenous sequence.

15 The polynucleotide encoding a polypeptide of the present invention may contain a secretory signal sequence that facilitates secretion of the protein. Typically, the signal sequence is positioned in the coding region of the polynucleotide to be expressed towards or at the 5' end of the coding region. The signal sequence may be homologous or heterologous to the polynucleotide of interest and may be homologous or heterologous to the cells to be transfected. Additionally, the signal sequence may be chemically synthesized using methods known in the art.

20 Any mode of administration of any of the above-described polynucleotides constructs can be used so long as the mode results in the expression of one or more molecules in an amount sufficient to provide a therapeutic effect. This includes direct needle injection, systemic injection, catheter infusion, biolistic injectors, particle accelerators (i.e., "gene guns"), gelfoam sponge depots, other commercially available depot materials, osmotic pumps (e.g., Alza minipumps), oral
25 or suppositorial solid (tablet or pill) pharmaceutical formulations, and decanting or topical applications during surgery. For example, direct injection of naked calcium phosphate-precipitated plasmid into rat liver and rat spleen or a protein-coated plasmid into the portal vein has resulted in gene expression of the foreign gene in the rat livers (Kaneda et al., Science 243:375 (1989)).

30 A preferred method of local administration is by direct injection. Preferably, a recombinant molecule of the present invention complexed with a delivery vehicle is administered by direct injection into or locally within the area of arteries. Administration of a composition locally within the area of arteries refers to injecting the composition centimeters and preferably, millimeters within arteries.

35 Another method of local administration is to contact a polynucleotide construct of the present invention in or around a surgical wound. For example, a patient can undergo surgery and

the polynucleotide construct can be coated on the surface of tissue inside the wound or the construct can be injected into areas of tissue inside the wound.

Therapeutic compositions useful in systemic administration, include recombinant molecules of the present invention complexed to a targeted delivery vehicle of the present invention. Suitable delivery vehicles for use with systemic administration comprise liposomes comprising ligands for targeting the vehicle to a particular site. In specific embodiments, suitable delivery vehicles for use with systemic administration comprise liposomes comprising polypeptides of the invention for targeting the vehicle to a particular site.

Preferred methods of systemic administration, include intravenous injection, aerosol, oral and percutaneous (topical) delivery. Intravenous injections can be performed using methods standard in the art. Aerosol delivery can also be performed using methods standard in the art (see, for example, Stribling et al., Proc. Natl. Acad. Sci. USA 189:11277-11281, 1992, which is incorporated herein by reference). Oral delivery can be performed by complexing a polynucleotide construct of the present invention to a carrier capable of withstanding degradation by digestive enzymes in the gut of an animal. Examples of such carriers, include plastic capsules or tablets, such as those known in the art. Topical delivery can be performed by mixing a polynucleotide construct of the present invention with a lipophilic reagent (e.g., DMSO) that is capable of passing into the skin.

Determining an effective amount of substance to be delivered can depend upon a number of factors including, for example, the chemical structure and biological activity of the substance, the age and weight of the animal, the precise condition requiring treatment and its severity, and the route of administration. The frequency of treatments depends upon a number of factors, such as the amount of polynucleotide constructs administered per dose, as well as the health and history of the subject. The precise amount, number of doses, and timing of doses will be determined by the attending physician or veterinarian.

Therapeutic compositions of the present invention can be administered to any animal, preferably to mammals and birds. Preferred mammals include humans, dogs, cats, mice, rats, rabbits sheep, cattle, horses and pigs, with humans being particularly preferred.

Biological Activities

Polynucleotides or polypeptides, or agonists or antagonists of the present invention, can be used in assays to test for one or more biological activities. If these polynucleotides or polypeptides, or agonists or antagonists of the present invention, do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides and polypeptides, and agonists or antagonists could be used to treat the associated disease.

Members of the secreted family of proteins are believed to be involved in biological activities associated with, for example, cellular signaling. Accordingly, compositions of the invention (including polynucleotides, polypeptides and antibodies of the invention, and fragments and variants thereof) may be used in diagnosis, prognosis, prevention and/or treatment of diseases and/or disorders associated with aberrant activity of secreted polypeptides.

In preferred embodiments, compositions of the invention (including polynucleotides, polypeptides and antibodies of the invention, and fragments and variants thereof) may be used in the diagnosis, prognosis, prevention, treatment, and/or amelioration of cancer and other hyperproliferative diseases and/or disorders (e.g., as described in the "Hyperproliferative Disorders"). In certain embodiments, a polypeptide of the invention, or polynucleotides, antibodies, agonists, or antagonists corresponding to that polypeptide, may be used to diagnose and/or prognosticate diseases and/or disorders associated with the tissue(s) in which the polypeptide of the invention is expressed including one, two, three, four, five, or more tissues disclosed in Table 1B.2, column 5 (Tissue Distribution Library Code).

Thus, polynucleotides, translation products and antibodies of the invention are useful in the diagnosis, detection, prevention, prognostication, and/or treatment of diseases and/or disorders associated with activities that include, but are not limited to, prohormone activation, neurotransmitter activity, cellular signaling, cellular proliferation, cellular differentiation, and cell migration.

More generally, polynucleotides, translation products and antibodies corresponding to this gene may be useful for the diagnosis, prognosis, prevention, treatment and/or amelioration of diseases and/or disorders associated with the following system or systems.

Immune Activity

Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in preventing, diagnosing, prognosticating, treating, and/or ameliorating diseases, disorders, and/or conditions of the immune system, by, for example, activating or inhibiting the proliferation, differentiation, or mobilization (chemotaxis) of immune cells. Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and macrophages) and lymphoid (B and T lymphocytes) cells from pluripotent stem cells. The etiology of these immune diseases, disorders, and/or conditions may be genetic, somatic, such as cancer and some autoimmune diseases, acquired (e.g., by chemotherapy or toxins), or infectious. Moreover, polynucleotides, polypeptides, antibodies,

and/or agonists or antagonists of the present invention can be used as a marker or detector of a particular immune system disease or disorder.

In another embodiment, a polypeptide of the invention, or polynucleotides, antibodies, agonists, or antagonists corresponding to that polypeptide, may be used to treat diseases and disorders of the immune system and/or to inhibit or enhance an immune response generated by cells associated with the tissue(s) in which the polypeptide of the invention is expressed, including one, two, three, four, five, or more tissues disclosed in Table 1B.2, column 5 (Tissue Distribution Library Code).

Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in preventing, diagnosing, prognosticating, treating and/or ameliorating immunodeficiencies, including both congenital and acquired immunodeficiencies. Examples of B cell immunodeficiencies in which immunoglobulin levels B cell function and/or B cell numbers are decreased include: X-linked agammaglobulinemia (Bruton's disease), X-linked infantile agammaglobulinemia, X-linked immunodeficiency with hyper IgM, non X-linked immunodeficiency with hyper IgM, X-linked lymphoproliferative syndrome (XLP), agammaglobulinemia including congenital and acquired agammaglobulinemia, adult onset agammaglobulinemia, late-onset agammaglobulinemia, dysgammaglobulinemia, hypogammaglobulinemia, unspecified hypogammaglobulinemia, recessive agammaglobulinemia (Swiss type), Selective IgM deficiency, selective IgA deficiency, selective IgG subclass deficiencies, IgG subclass deficiency (with or without IgA deficiency), Ig deficiency with increased IgM, IgG and IgA deficiency with increased IgM, antibody deficiency with normal or elevated Igs, Ig heavy chain deletions, kappa chain deficiency, B cell lymphoproliferative disorder (BLPD), common variable immunodeficiency (CVID), common variable immunodeficiency (CVI) (acquired), and transient hypogammaglobulinemia of infancy.

In specific embodiments, ataxia-telangiectasia or conditions associated with ataxia-telangiectasia are detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated using the polypeptides or polynucleotides of the invention, and/or agonists or antagonists thereof.

Examples of congenital immunodeficiencies in which T cell and/or B cell function and/or number is decreased include, but are not limited to: DiGeorge anomaly, severe combined immunodeficiencies (SCID) (including, but not limited to, X-linked SCID, autosomal recessive SCID, adenosine deaminase deficiency, purine nucleoside phosphorylase (PNP) deficiency, Class

II MHC deficiency (Bare lymphocyte syndrome), Wiskott-Aldrich syndrome, and ataxia telangiectasia), thymic hypoplasia, third and fourth pharyngeal pouch syndrome, 22q11.2 deletion, chronic mucocutaneous candidiasis, natural killer cell deficiency (NK), idiopathic CD4+ T-lymphocytopenia, immunodeficiency with predominant T cell defect (unspecified), and
5 unspecified immunodeficiency of cell mediated immunity.

In specific embodiments, DiGeorge anomaly or conditions associated with DiGeorge anomaly are prevented, detected, diagnosed, prognosticated, treated and/or ameliorated using polypeptides or polynucleotides of the invention, or antagonists or agonists thereof.

Other immunodeficiencies that may be prevented, detected, diagnosed, prognosticated,
10 treated and/or ameliorated using polypeptides or polynucleotides of the invention, and/or agonists or antagonists thereof, include, but are not limited to, chronic granulomatous disease, Chédiak-Higashi syndrome, myeloperoxidase deficiency, leukocyte glucose-6-phosphate dehydrogenase deficiency, X-linked lymphoproliferative syndrome (XLP), leukocyte adhesion deficiency, complement component deficiencies (including C1, C2, C3, C4, C5, C6, C7, C8 and/or C9
15 deficiencies), reticular dysgenesis, thymic aplasia, immunodeficiency with thymoma, severe congenital leukopenia, dysplasia with immunodeficiency, neonatal neutropenia, short limbed dwarfism, and Nezelof syndrome-combined immunodeficiency with Igs.

In a preferred embodiment, the immunodeficiencies and/or conditions associated with the immunodeficiencies recited above are prevented, detected, diagnosed, prognosticated, treated
20 and/or ameliorated using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention.

In a preferred embodiment polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention could be used as an agent to boost immunoresponsiveness among immunodeficient individuals. In specific embodiments, polynucleotides, polypeptides,
25 antibodies, and/or agonists or antagonists of the present invention could be used as an agent to boost immunoresponsiveness among B cell and/or T cell immunodeficient individuals.

The polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in preventing, detecting, diagnosing, prognosticating, treating and/or ameliorating autoimmune disorders. Many autoimmune disorders result from inappropriate
30 recognition of self as foreign material by immune cells. This inappropriate recognition results in an immune response leading to the destruction of the host tissue. Therefore, the administration of

polynucleotides and polypeptides of the invention that can inhibit an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders.

Autoimmune diseases or disorders that may be prevented, detected, diagnosed, prognosticated, treated, and/or ameliorated by polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention include, but are not limited to, one or more of the following: systemic lupus erythematosus, rheumatoid arthritis, ankylosing spondylitis, multiple sclerosis, autoimmune thyroiditis, Hashimoto's thyroiditis, autoimmune hemolytic anemia, hemolytic anemia, thrombocytopenia, autoimmune thrombocytopenia purpura, autoimmune neonatal thrombocytopenia, idiopathic thrombocytopenia purpura, purpura (e.g., Henloch-Schoenlein purpura), autoimmune cytopenia, Goodpasture's syndrome, Pemphigus vulgaris, myasthenia gravis, Grave's disease (hyperthyroidism), and insulin-resistant diabetes mellitus.

Additional disorders that are likely to have an autoimmune component that may be prevented, detected, diagnosed, prognosticated, treated and/or ameliorated with the compositions of the invention include, but are not limited to, type II collagen-induced arthritis, antiphospholipid syndrome, dermatitis, allergic encephalomyelitis, myocarditis, relapsing polychondritis, rheumatic heart disease, neuritis, uveitis ophthalmia, polyendocrinopathies, Reiter's Disease, Stiff-Man Syndrome, autoimmune pulmonary inflammation, autism, Guillain-Barre Syndrome, insulin dependent diabetes mellitus, and autoimmune inflammatory eye disorders.

Additional disorders that are likely to have an autoimmune component that may be prevented, detected, diagnosed, prognosticated, treated and/or ameliorated with the compositions of the invention include, but are not limited to, scleroderma with anti-collagen antibodies (often characterized, e.g., by nucleolar and other nuclear antibodies), mixed connective tissue disease (often characterized, e.g., by antibodies to extractable nuclear antigens (e.g., ribonucleoprotein)), polymyositis (often characterized, e.g., by nonhistone ANA), pernicious anemia (often characterized, e.g., by antiparietal cell, microsomes, and intrinsic factor antibodies), idiopathic Addison's disease (often characterized, e.g., by humoral and cell-mediated adrenal cytotoxicity, infertility (often characterized, e.g., by antispermatozoal antibodies), glomerulonephritis (often characterized, e.g., by glomerular basement membrane antibodies or immune complexes), bullous pemphigoid (often characterized, e.g., by IgG and complement in basement membrane), Sjogren's syndrome (often characterized, e.g., by multiple tissue antibodies, and/or a specific nonhistone

ANA (SS-B)), diabetes mellitus (often characterized, e.g., by cell-mediated and humoral islet cell antibodies), and adrenergic drug resistance (including adrenergic drug resistance with asthma or cystic fibrosis) (often characterized, e.g., by beta-adrenergic receptor antibodies).

Additional disorders that may have an autoimmune component that may be prevented,
5 detected, diagnosed, prognosticated, treated and/or ameliorated with the compositions of the invention include, but are not limited to, chronic active hepatitis (often characterized, e.g., by smooth muscle antibodies), primary biliary cirrhosis (often characterized, e.g., by mitochondria antibodies), other endocrine gland failure (often characterized, e.g., by specific tissue antibodies in some cases), vitiligo (often characterized, e.g., by melanocyte antibodies), vasculitis (often
10 characterized, e.g., by Ig and complement in vessel walls and/or low serum complement), post-MI (often characterized, e.g., by myocardial antibodies), cardiomyopathy syndrome (often characterized, e.g., by myocardial antibodies), urticaria (often characterized, e.g., by IgG and IgM antibodies to IgE), atopic dermatitis (often characterized, e.g., by IgG and IgM antibodies to IgE), asthma (often characterized, e.g., by IgG and IgM antibodies to IgE), and many other inflammatory,
15 granulomatous, degenerative, and atrophic disorders.

In a preferred embodiment, the autoimmune diseases and disorders and/or conditions associated with the diseases and disorders recited above are prevented, detected, diagnosed, prognosticated, treated and/or ameliorated using for example, antagonists or agonists, polypeptides or polynucleotides, or antibodies of the present invention. In a specific preferred embodiment,
20 rheumatoid arthritis is prevented, detected, diagnosed, prognosticated, treated and/or ameliorated using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention.

In another specific preferred embodiment, systemic lupus erythematosus is prevented, detected, diagnosed, prognosticated, treated and/or ameliorated using polynucleotides,
25 polypeptides, antibodies, and/or agonists or antagonists of the present invention. In another specific preferred embodiment, idiopathic thrombocytopenia purpura is prevented, detected, diagnosed, prognosticated, treated and/or ameliorated using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention.

In another specific preferred embodiment IgA nephropathy is prevented, detected,
30 diagnosed, prognosticated, treated and/or ameliorated using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention.

In a preferred embodiment, the autoimmune diseases and disorders and/or conditions associated with the diseases and disorders recited above are prevented, detected, diagnosed, prognosticated, treated and/or ameliorated using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention

5 In preferred embodiments, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a immunosuppressive agent(s).

Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in detecting, preventing, diagnosing, prognosticating, treating, and/or ameliorating diseases, disorders, and/or conditions of hematopoietic cells. Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat or prevent those diseases, disorders, and/or conditions associated with a decrease in certain (or many) types hematopoietic cells, including but not limited to, leukopenia, neutropenia, anemia, and thrombocytopenia. Alternatively, Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat or prevent those diseases, disorders, and/or conditions associated with an increase in certain (or many) types of hematopoietic cells, including but not limited to, histiocytosis.

Allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated using polypeptides, antibodies, or polynucleotides of the invention, and/or agonists or antagonists thereof. Moreover, these molecules can be used to treat, prevent, prognose, and/or diagnose anaphylaxis, hypersensitivity to an antigenic molecule, or blood group incompatibility.

Additionally, polypeptides or polynucleotides of the invention, and/or agonists or antagonists thereof, may be used to detect, prevent, diagnose, prognosticate, treat, and/or ameliorate IgE-mediated allergic reactions. Such allergic reactions include, but are not limited to, asthma, rhinitis, and eczema. In specific embodiments, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be used to modulate IgE concentrations in vitro or in vivo.

30 Moreover, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention have uses in the detection, prevention, diagnosis, prognostication, treatment,

and/or amelioration of inflammatory conditions. For example, since polypeptides, antibodies, or polynucleotides of the invention, and/or agonists or antagonists of the invention may inhibit the activation, proliferation and/or differentiation of cells involved in an inflammatory response, these molecules can be used to prevent and/or treat chronic and acute inflammatory conditions. Such inflammatory conditions include, but are not limited to, for example, inflammation associated with infection (e.g., septic shock, sepsis, or systemic inflammatory response syndrome), ischemia-reperfusion injury, endotoxin lethality, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease, Crohn's disease, over production of cytokines (e.g., TNF or IL-1.), respiratory disorders (e.g., asthma and allergy); gastrointestinal disorders (e.g., inflammatory bowel disease); cancers (e.g., gastric, ovarian, lung, bladder, liver, and breast); CNS disorders (e.g., multiple sclerosis; ischemic brain injury and/or stroke, traumatic brain injury, neurodegenerative disorders (e.g., Parkinson's disease and Alzheimer's disease); AIDS-related dementia; and prion disease); cardiovascular disorders (e.g., atherosclerosis, myocarditis, cardiovascular disease, and cardiopulmonary bypass complications); as well as many additional diseases, conditions, and disorders that are characterized by inflammation (e.g., hepatitis, rheumatoid arthritis, gout, trauma, pancreatitis, sarcoidosis, dermatitis, renal ischemia-reperfusion injury, Grave's disease, systemic lupus erythematosus, diabetes mellitus, and allogenic transplant rejection).

Because inflammation is a fundamental defense mechanism, inflammatory disorders can effect virtually any tissue of the body. Accordingly, polynucleotides, polypeptides, and antibodies of the invention, as well as agonists or antagonists thereof, have uses in the treatment of tissue-specific inflammatory disorders, including, but not limited to, adrenalitis, alveolitis, angiocholecystitis, appendicitis, balanitis, blepharitis, bronchitis, bursitis, carditis, cellulitis, cervicitis, cholecystitis, chondritis, cochitis, colitis, conjunctivitis, cystitis, dermatitis, diverticulitis, encephalitis, endocarditis, esophagitis, eustachitis, fibrositis, folliculitis, gastritis, gastroenteritis, gingivitis, glossitis, hepatosplenitis, keratitis, labyrinthitis, laryngitis, lymphangitis, mastitis, media otitis, meningitis, metritis, mucitis, myocarditis, myositis, myringitis, nephritis, neuritis, orchitis, osteochondritis, otitis, pericarditis, peritendonitis, peritonitis, pharyngitis, phlebitis, poliomyelitis, prostatitis, pulpitis, retinitis, rhinitis, salpingitis, scleritis, sclerochoroiditis, scrotitis, sinusitis, spondylitis, steatitis, stomatitis, synovitis, syringitis, tendonitis, tonsillitis, urethritis, and vaginitis.

In specific embodiments, polypeptides, antibodies, or polynucleotides of the invention, and/or agonists or antagonists thereof, are useful to detect, prevent, diagnose, prognosticate, treat, and/or ameliorate organ transplant rejections and graft-versus-host disease. Organ rejection occurs by host immune cell destruction of the transplanted tissue through an immune response. Similarly, 5 an immune response is also involved in GVHD, but, in this case, the foreign transplanted immune cells destroy the host tissues. Polypeptides, antibodies, or polynucleotides of the invention, and/or agonists or antagonists thereof, that inhibit an immune response, particularly the activation, proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing organ rejection or GVHD. In specific embodiments, polypeptides, antibodies, or polynucleotides 10 of the invention, and/or agonists or antagonists thereof, that inhibit an immune response, particularly the activation, proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing experimental allergic and hyperacute xenograft rejection.

In other embodiments, polypeptides, antibodies, or polynucleotides of the invention, and/or agonists or antagonists thereof, are useful to detect, prevent, diagnose, prognosticate, treat, 15 and/or ameliorate immune complex diseases, including, but not limited to, serum sickness, post streptococcal glomerulonephritis, polyarteritis nodosa, and immune complex-induced vasculitis.

Polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the invention can be used to treat, detect, and/or prevent infectious agents. For example, by increasing the immune response, particularly increasing the proliferation activation and/or differentiation of B 20 and/or T cells, infectious diseases may be treated, detected, and/or prevented. The immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may also directly inhibit the infectious agent (refer to section of application listing infectious agents, etc), without necessarily eliciting an immune 25 response.

In another embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a vaccine adjuvant that enhances immune responsiveness to an antigen. In a specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an adjuvant to enhance tumor- 30 specific immune responses.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an adjuvant to enhance anti-viral immune responses. Anti-viral immune responses that may be enhanced using the compositions of the invention as an adjuvant, include virus and virus associated diseases or symptoms described herein or otherwise known in the art. In specific embodiments, the compositions of the invention are used as an adjuvant to enhance an immune response to a virus, disease, or symptom selected from the group consisting of: AIDS, meningitis, Dengue, EBV, and hepatitis (e.g., hepatitis B). In another specific embodiment, the compositions of the invention are used as an adjuvant to enhance an immune response to a virus, disease, or symptom selected from the group consisting of: HIV/AIDS, respiratory syncytial virus, Dengue, rotavirus, Japanese B encephalitis, influenza A and B, parainfluenza, measles, cytomegalovirus, rabies, Junin, Chikungunya, Rift Valley Fever, herpes simplex, and yellow fever.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an adjuvant to enhance anti-bacterial or anti-fungal immune responses. Anti-bacterial or anti-fungal immune responses that may be enhanced using the compositions of the invention as an adjuvant, include bacteria or fungus and bacteria or fungus associated diseases or symptoms described herein or otherwise known in the art. In specific embodiments, the compositions of the invention are used as an adjuvant to enhance an immune response to a bacteria or fungus, disease, or symptom selected from the group consisting of: tetanus, Diphtheria, botulism, and meningitis type B.

In another specific embodiment, the compositions of the invention are used as an adjuvant to enhance an immune response to a bacteria or fungus, disease, or symptom selected from the group consisting of: *Vibrio cholerae*, *Mycobacterium leprae*, *Salmonella typhi*, *Salmonella paratyphi*, *Meisseria meningitidis*, *Streptococcus pneumoniae*, Group B streptococcus, *Shigella spp.*, Enterotoxigenic *Escherichia coli*, Enterohemorrhagic *E. coli*, and *Borrelia burgdorferi*.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an adjuvant to enhance anti-parasitic immune responses. Anti-parasitic immune responses that may be enhanced using the compositions of the invention as an adjuvant, include parasite and parasite associated diseases or symptoms described herein or otherwise known in the art. In specific embodiments, the compositions of the invention are used as an adjuvant to enhance an immune response to a parasite. In another specific

embodiment, the compositions of the invention are used as an adjuvant to enhance an immune response to Plasmodium (malaria) or Leishmania.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may also be employed to treat infectious diseases including
5 silicosis, sarcoidosis, and idiopathic pulmonary fibrosis; for example, by preventing the recruitment and activation of mononuclear phagocytes.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an antigen for the generation of antibodies to inhibit or enhance immune mediated responses against polypeptides of the invention.

10 In one embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are administered to an animal (e.g., mouse, rat, rabbit, hamster, guinea pig, pigs, micro-pig, chicken, camel, goat, horse, cow, sheep, dog, cat, non-human primate, and human, most preferably human) to boost the immune system to produce increased quantities of one or more antibodies (e.g., IgG, IgA, IgM, and IgE), to induce higher affinity
15 antibody production and immunoglobulin class switching (e.g., IgG, IgA, IgM, and IgE), and/or to increase an immune response.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a stimulator of B cell responsiveness to pathogens.

20 In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an activator of T cells.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent that elevates the immune status of an individual prior to their receipt of immunosuppressive therapies.

25 In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to induce higher affinity antibodies.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to increase serum immunoglobulin concentrations.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to accelerate recovery of immunocompromised individuals.

5 In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to boost immunoresponsiveness among aged populations and/or neonates.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an immune system enhancer prior to, during, or after bone marrow transplant and/or other transplants (e.g., allogeneic or xenogeneic organ
10 transplantation). With respect to transplantation, compositions of the invention may be administered prior to, concomitant with, and/or after transplantation. In a specific embodiment, compositions of the invention are administered after transplantation, prior to the beginning of recovery of T-cell populations. In another specific embodiment, compositions of the invention are first administered after transplantation after the beginning of recovery of T cell populations, but
15 prior to full recovery of B cell populations.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to boost immunoresponsiveness among individuals having an acquired loss of B cell function. Conditions resulting in an acquired loss of B cell function that may be ameliorated or treated by administering the polypeptides, antibodies,
20 polynucleotides and/or agonists or antagonists thereof, include, but are not limited to, HIV Infection, AIDS, bone marrow transplant, and B cell chronic lymphocytic leukemia (CLL).

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to boost immunoresponsiveness among individuals having a temporary immune deficiency. Conditions resulting in a temporary immune
25 deficiency that may be ameliorated or treated by administering the polypeptides, antibodies, polynucleotides and/or agonists or antagonists thereof, include, but are not limited to, recovery from viral infections (e.g., influenza), conditions associated with malnutrition, recovery from infectious mononucleosis, or conditions associated with stress, recovery from measles, recovery from blood transfusion, and recovery from surgery.

30 In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a regulator of antigen presentation by

monocytes, dendritic cells, and/or B-cells. In one embodiment, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention enhance antigen presentation or antagonizes antigen presentation in vitro or in vivo. Moreover, in related embodiments, said enhancement or antagonism of antigen presentation may be useful as an anti-tumor treatment or to
5 modulate the immune system.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to direct an individual's immune system towards development of a humoral response (i.e. TH2) as opposed to a TH1 cellular response.

10 In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a means to induce tumor proliferation and thus make it more susceptible to anti-neoplastic agents. For example, multiple myeloma is a slowly dividing disease and is thus refractory to virtually all anti-neoplastic regimens. If these cells were forced to proliferate more rapidly their susceptibility profile would likely change.

15 In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a stimulator of B cell production in pathologies such as AIDS, chronic lymphocyte disorder and/or Common Variable Immunodeficiency.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a therapy for generation and/or regeneration of
20 lymphoid tissues following surgery, trauma or genetic defect. In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used in the pretreatment of bone marrow samples prior to transplant.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a gene-based therapy for genetically inherited
25 disorders resulting in immuno-incompetence/immunodeficiency such as observed among SCID patients.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a means of activating monocytes/macrophages to defend against parasitic diseases that effect monocytes such as Leishmania.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a means of regulating secreted cytokines that are elicited by polypeptides of the invention.

5 In another embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used in one or more of the applications described herein, as they may apply to veterinary medicine.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a means of blocking various aspects of immune responses to foreign agents or self. Examples of diseases or conditions in which blocking of
10 certain aspects of immune responses may be desired include autoimmune disorders such as lupus, and arthritis, as well as immunoresponsiveness to skin allergies, inflammation, bowel disease, injury and diseases/disorders associated with pathogens.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a therapy for preventing the B cell proliferation
15 and Ig secretion associated with autoimmune diseases such as idiopathic thrombocytopenic purpura, systemic lupus erythematosus and multiple sclerosis.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a inhibitor of B and/or T cell migration in endothelial cells. This activity disrupts tissue architecture or cognate responses and is useful, for
20 example in disrupting immune responses, and blocking sepsis.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a therapy for chronic hypergammaglobulinemia evident in such diseases as monoclonal gammopathy of undetermined significance (MGUS), Waldenstrom's disease, related idiopathic monoclonal gammopathies, and plasmacytomas.

25 In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may be employed for instance to inhibit polypeptide chemotaxis and activation of macrophages and their precursors, and of neutrophils, basophils, B lymphocytes and some T-cell subsets, e.g., activated and CD8 cytotoxic T cells and natural killer cells, in certain autoimmune and chronic inflammatory and infective diseases. Examples of
30 autoimmune diseases are described herein and include multiple sclerosis, and insulin-dependent diabetes.

The polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may also be employed to treat idiopathic hyper-eosinophilic syndrome by, for example, preventing eosinophil production and migration.

5 In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used to enhance or inhibit complement mediated cell lysis.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used to enhance or inhibit antibody dependent cellular cytotoxicity.

10 In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may also be employed for treating atherosclerosis, for example, by preventing monocyte infiltration in the artery wall.

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may be employed to treat adult respiratory distress
15 syndrome (ARDS).

In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may be useful for stimulating wound and tissue repair, stimulating angiogenesis, and/or stimulating the repair of vascular or lymphatic diseases or disorders. Additionally, agonists and antagonists of the invention may be used to stimulate the
20 regeneration of mucosal surfaces.

In a specific embodiment, polynucleotides or polypeptides, and/or agonists thereof are used to detect, prevent, diagnose, prognosticate, treat, and/or ameliorate a disorder characterized by primary or acquired immunodeficiency, deficient serum immunoglobulin production, recurrent infections, and/or immune system dysfunction. Moreover, polynucleotides or polypeptides, and/or
25 agonists thereof may be used to treat or prevent infections of the joints, bones, skin, and/or parotid glands, blood-borne infections (e.g., sepsis, meningitis, septic arthritis, and/or osteomyelitis), autoimmune diseases (e.g., those disclosed herein), inflammatory disorders, and malignancies, and/or any disease or disorder or condition associated with these infections, diseases, disorders and/or malignancies) including, but not limited to, CVID, other primary immune deficiencies,
30 HIV disease, CLL, recurrent bronchitis, sinusitis, otitis media, conjunctivitis, pneumonia, hepatitis, meningitis, herpes zoster (e.g., severe herpes zoster), and/or pneumocystis carinii. Other

diseases and disorders that may be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated with polynucleotides or polypeptides, and/or agonists of the present invention include, but are not limited to, HIV infection, HTLV-BLV infection, lymphopenia, phagocyte bactericidal dysfunction anemia, thrombocytopenia, and hemoglobinuria.

5 In another embodiment, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention are used to treat, and/or diagnose an individual having common variable immunodeficiency disease ("CVID"; also known as "acquired agammaglobulinemia" and "acquired hypogammaglobulinemia") or a subset of this disease.

10 In a specific embodiment, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be used to detect, prevent, diagnose, prognosticate, treat, and/or ameliorate cancers or neoplasms including immune cell or immune tissue-related cancers or neoplasms. Examples of cancers or neoplasms that may be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated by polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention include, but are not limited to, acute myelogenous
15 leukemia, chronic myelogenous leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, acute lymphocytic anemia (ALL) Chronic lymphocyte leukemia, plasmacytomas, multiple myeloma, Burkitt's lymphoma, EBV-transformed diseases, and/or diseases and disorders described in the section entitled "Hyperproliferative Disorders" elsewhere herein.

20 In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a therapy for decreasing cellular proliferation of Large B-cell Lymphomas.

 In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a means of decreasing the involvement of B cells and Ig associated with Chronic Myelogenous Leukemia.

25 In specific embodiments, the compositions of the invention are used as an agent to boost immunoresponsiveness among B cell immunodeficient individuals, such as, for example, an individual who has undergone a partial or complete splenectomy.

 Antagonists of the invention include, for example, binding and/or inhibitory antibodies, antisense nucleic acids, ribozymes or soluble forms of the polypeptides of the present invention
30 (e.g., Fc fusion protein; see, e.g., Example 9). Agonists of the invention include, for example, binding or stimulatory antibodies, and soluble forms of the polypeptides (e.g., Fc fusion proteins;

see, e.g., Example 9). polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may be employed in a composition with a pharmaceutically acceptable carrier, e.g., as described herein.

In another embodiment, polypeptides, antibodies, polynucleotides and/or agonists or
5 antagonists of the present invention are administered to an animal (including, but not limited to, those listed above, and also including transgenic animals) incapable of producing functional endogenous antibody molecules or having an otherwise compromised endogenous immune system, but which is capable of producing human immunoglobulin molecules by means of a reconstituted or partially reconstituted immune system from another animal (see, e.g., published
10 PCT Application Nos. WO98/24893, WO/9634096, WO/9633735, and WO/9110741). Administration of polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention to such animals is useful for the generation of monoclonal antibodies against the polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention.

15

Hyperproliferative Disorders

In certain embodiments, polynucleotides or polypeptides, or agonists or antagonists of the present invention can be used to treat or detect hyperproliferative disorders, including neoplasms. Polynucleotides or polypeptides, or agonists or antagonists of the present invention may inhibit the
20 proliferation of the disorder through direct or indirect interactions. Alternatively, Polynucleotides or polypeptides, or agonists or antagonists of the present invention may proliferate other cells which can inhibit the hyperproliferative disorder.

For example, by increasing an immune response, particularly increasing antigenic qualities of the hyperproliferative disorder or by proliferating, differentiating, or mobilizing T-cells,
25 hyperproliferative disorders can be treated. This immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, decreasing an immune response may also be a method of treating hyperproliferative disorders, such as a chemotherapeutic agent.

Examples of hyperproliferative disorders that can be treated or detected by
30 polynucleotides or polypeptides, or agonists or antagonists of the present invention include, but are not limited to neoplasms located in the: colon, abdomen, bone, breast, digestive system, liver, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous (central and peripheral), lymphatic system, pelvis, skin, soft tissue, spleen, thorax, and urogenital tract.

Similarly, other hyperproliferative disorders can also be treated or detected by polynucleotides or polypeptides, or agonists or antagonists of the present invention. Examples of such hyperproliferative disorders include, but are not limited to: Acute Childhood Lymphoblastic Leukemia, Acute Lymphoblastic Leukemia, Acute Lymphocytic Leukemia, Acute Myeloid Leukemia, Adrenocortical Carcinoma, Adult (Primary) Hepatocellular Cancer, Adult (Primary) Liver Cancer, Adult Acute Lymphocytic Leukemia, Adult Acute Myeloid Leukemia, Adult Hodgkin's Disease, Adult Hodgkin's Lymphoma, Adult Lymphocytic Leukemia, Adult Non-Hodgkin's Lymphoma, Adult Primary Liver Cancer, Adult Soft Tissue Sarcoma, AIDS-Related Lymphoma, AIDS-Related Malignancies, Anal Cancer, Astrocytoma, Bile Duct Cancer, Bladder Cancer, Bone Cancer, Brain Stem Glioma, Brain Tumors, Breast Cancer, Cancer of the Renal Pelvis and Ureter, Central Nervous System (Primary) Lymphoma, Central Nervous System Lymphoma, Cerebellar Astrocytoma, Cerebral Astrocytoma, Cervical Cancer, Childhood (Primary) Hepatocellular Cancer, Childhood (Primary) Liver Cancer, Childhood Acute Lymphoblastic Leukemia, Childhood Acute Myeloid Leukemia, Childhood Brain Stem Glioma, Childhood Cerebellar Astrocytoma, Childhood Cerebral Astrocytoma, Childhood Extracranial Germ Cell Tumors, Childhood Hodgkin's Disease, Childhood Hodgkin's Lymphoma, Childhood Hypothalamic and Visual Pathway Glioma, Childhood Lymphoblastic Leukemia, Childhood Medulloblastoma, Childhood Non-Hodgkin's Lymphoma, Childhood Pineal and Supratentorial Primitive Neuroectodermal Tumors, Childhood Primary Liver Cancer, Childhood Rhabdomyosarcoma, Childhood Soft Tissue Sarcoma, Childhood Visual Pathway and Hypothalamic Glioma, Chronic Lymphocytic Leukemia, Chronic Myelogenous Leukemia, Colon Cancer, Cutaneous T-Cell Lymphoma, Endocrine Pancreas Islet Cell Carcinoma, Endometrial Cancer, Ependymoma, Epithelial Cancer, Esophageal Cancer, Ewing's Sarcoma and Related Tumors, Exocrine Pancreatic Cancer, Extracranial Germ Cell Tumor, Extragenital Germ Cell Tumor, Extrahepatic Bile Duct Cancer, Eye Cancer, Female Breast Cancer, Gaucher's Disease, Gallbladder Cancer, Gastric Cancer, Gastrointestinal Carcinoid Tumor, Gastrointestinal Tumors, Germ Cell Tumors, Gestational Trophoblastic Tumor, Hairy Cell Leukemia, Head and Neck Cancer, Hepatocellular Cancer, Hodgkin's Disease, Hodgkin's Lymphoma, Hypergammaglobulinemia, Hypopharyngeal Cancer, Intestinal Cancers, Intraocular Melanoma, Islet Cell Carcinoma, Islet Cell Pancreatic Cancer, Kaposi's Sarcoma, Kidney Cancer, Laryngeal Cancer, Lip and Oral Cavity Cancer, Liver Cancer, Lung Cancer, Lymphoproliferative Disorders, Macroglobulinemia, Male Breast Cancer, Malignant Mesothelioma, Malignant Thymoma, Medulloblastoma, Melanoma, Mesothelioma, Metastatic Occult Primary Squamous Neck Cancer, Metastatic Primary Squamous Neck Cancer, Metastatic Squamous Neck Cancer, Multiple Myeloma, Multiple Myeloma/Plasma Cell Neoplasm, Myelodysplastic Syndrome, Myelogenous Leukemia, Myeloid Leukemia, Myeloproliferative Disorders, Nasal Cavity and Paranasal Sinus Cancer, Nasopharyngeal Cancer, Neuroblastoma, Non-Hodgkin's Lymphoma During Pregnancy,

Nonmelanoma Skin Cancer, Non-Small Cell Lung Cancer, Occult Primary Metastatic Squamous Neck Cancer, Oropharyngeal Cancer, Osteo-/Malignant Fibrous Sarcoma, Osteosarcoma/Malignant Fibrous Histiocytoma, Osteosarcoma/Malignant Fibrous Histiocytoma of Bone, Ovarian Epithelial Cancer, Ovarian Germ Cell Tumor, Ovarian Low Malignant Potential
 5 Tumor, Pancreatic Cancer, Paraproteinemias, Purpura, Parathyroid Cancer, Penile Cancer, Pheochromocytoma, Pituitary Tumor, Plasma Cell Neoplasm/Multiple Myeloma, Primary Central Nervous System Lymphoma, Primary Liver Cancer, Prostate Cancer, Rectal Cancer, Renal Cell Cancer, Renal Pelvis and Ureter Cancer, Retinoblastoma, Rhabdomyosarcoma, Salivary Gland Cancer, Sarcoidosis Sarcomas, Sezary Syndrome, Skin Cancer, Small Cell Lung Cancer, Small
 10 Intestine Cancer, Soft Tissue Sarcoma, Squamous Neck Cancer, Stomach Cancer, Supratentorial Primitive Neuroectodermal and Pineal Tumors, T-Cell Lymphoma, Testicular Cancer, Thymoma, Thyroid Cancer, Transitional Cell Cancer of the Renal Pelvis and Ureter, Transitional Renal Pelvis and Ureter Cancer, Trophoblastic Tumors, Ureter and Renal Pelvis Cell Cancer, Urethral Cancer, Uterine Cancer, Uterine Sarcoma, Vaginal Cancer, Visual Pathway and Hypothalamic Glioma,
 15 Vulvar Cancer, Waldenstrom's Macroglobulinemia, Wilms' Tumor, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

In another preferred embodiment, polynucleotides or polypeptides, or agonists or antagonists of the present invention are used to detect, prevent, diagnose, prognosticate, treat, and/or ameliorate premalignant conditions and to prevent progression to a neoplastic or malignant
 20 state, including but not limited to those disorders described above. Such uses are indicated in conditions known or suspected of preceding progression to neoplasia or cancer, in particular, where non-neoplastic cell growth consisting of hyperplasia, metaplasia, or most particularly, dysplasia has occurred (for review of such abnormal growth conditions, see Robbins and Angell, 1976, Basic Pathology, 2d Ed., W. B. Saunders Co., Philadelphia, pp. 68-79.)

Hyperplasia is a form of controlled cell proliferation, involving an increase in cell number in a tissue or organ, without significant alteration in structure or function. Hyperplastic disorders which can be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated with compositions of the invention (including polynucleotides, polypeptides, agonists or antagonists) include, but are not limited to, angiofollicular mediastinal lymph node hyperplasia, angiolymphoid
 30 hyperplasia with eosinophilia, atypical melanocytic hyperplasia, basal cell hyperplasia, benign giant lymph node hyperplasia, cementum hyperplasia, congenital adrenal hyperplasia, congenital sebaceous hyperplasia, cystic hyperplasia, cystic hyperplasia of the breast, denture hyperplasia, ductal hyperplasia, endometrial hyperplasia, fibromuscular hyperplasia, focal epithelial hyperplasia, gingival hyperplasia, inflammatory fibrous hyperplasia, inflammatory papillary
 35 hyperplasia, intravascular papillary endothelial hyperplasia, nodular hyperplasia of prostate, nodular regenerative hyperplasia, pseudoepitheliomatous hyperplasia, senile sebaceous hyperplasia, and verrucous hyperplasia.

Metaplasia is a form of controlled cell growth in which one type of adult or fully differentiated cell substitutes for another type of adult cell. Metaplastic disorders which can be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated with compositions of the invention (including polynucleotides, polypeptides, agonists or antagonists) include, but are not limited to, agnogenic myeloid metaplasia, apocrine metaplasia, atypical metaplasia, autoparenchymatous metaplasia, connective tissue metaplasia, epithelial metaplasia, intestinal metaplasia, metaplastic anemia, metaplastic ossification, metaplastic polyps, myeloid metaplasia, primary myeloid metaplasia, secondary myeloid metaplasia, squamous metaplasia, squamous metaplasia of amnion, and symptomatic myeloid metaplasia.

Dysplasia is frequently a forerunner of cancer, and is found mainly in the epithelia; it is the most disorderly form of non-neoplastic cell growth, involving a loss in individual cell uniformity and in the architectural orientation of cells. Dysplastic cells often have abnormally large, deeply stained nuclei, and exhibit pleomorphism. Dysplasia characteristically occurs where there exists chronic irritation or inflammation. Dysplastic disorders which can be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated with compositions of the invention (including polynucleotides, polypeptides, agonists or antagonists) include, but are not limited to, anhidrotic ectodermal dysplasia, anterofacial dysplasia, asphyxiating thoracic dysplasia, atriodigital dysplasia, bronchopulmonary dysplasia, cerebral dysplasia, cervical dysplasia, chondroectodermal dysplasia, cleidocranial dysplasia, congenital ectodermal dysplasia, craniodiaphysial dysplasia, craniocarpotarsal dysplasia, craniometaphysial dysplasia, dentin dysplasia, diaphysial dysplasia, ectodermal dysplasia, enamel dysplasia, encephalo-ophthalmic dysplasia, dysplasia epiphysialis hemimelia, dysplasia epiphysialis multiplex, dysplasia epiphysialis punctata, epithelial dysplasia, faciodeligitogenital dysplasia, familial fibrous dysplasia of jaws, familial white folded dysplasia, fibromuscular dysplasia, fibrous dysplasia of bone, florid osseous dysplasia, hereditary renal-retinal dysplasia, hidrotic ectodermal dysplasia, hypohidrotic ectodermal dysplasia, lymphopenic thymic dysplasia, mammary dysplasia, mandibulofacial dysplasia, metaphysial dysplasia, Mondini dysplasia, monostotic fibrous dysplasia, mucoepithelial dysplasia, multiple epiphysial dysplasia, oculoauriculovertebral dysplasia, oculodentodigital dysplasia, oculovertbral dysplasia, odontogenic dysplasia, ophthalmomandibulomelic dysplasia, periapical cemental dysplasia, polyostotic fibrous dysplasia, pseudoachondroplastic spondyloepiphysial dysplasia, retinal dysplasia, septo-optic dysplasia, spondyloepiphysial dysplasia, and ventriculoradial dysplasia.

Additional pre-neoplastic disorders which can be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated with compositions of the invention (including polynucleotides, polypeptides, agonists or antagonists) include, but are not limited to, benign dysproliferative disorders (e.g., benign tumors, fibrocystic conditions, tissue hypertrophy,

intestinal polyps, colon polyps, and esophageal dysplasia), leukoplakia, keratoses, Bowen's disease, Farmer's Skin, solar cheilitis, and solar keratosis.

In another embodiment, a polypeptide of the invention, or polynucleotides, antibodies, agonists, or antagonists corresponding to that polypeptide, may be used to diagnose and/or prognosticate disorders associated with the tissue(s) in which the polypeptide of the invention is expressed, including one, two, three, four, five, or more tissues disclosed in Table 1B.2, column 5 (Tissue Distribution Library Code).

In another embodiment, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention conjugated to a toxin or a radioactive isotope, as described herein, may be used to treat cancers and neoplasms, including, but not limited to those described herein. In a further preferred embodiment, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention conjugated to a toxin or a radioactive isotope, as described herein, may be used to treat acute myelogenous leukemia.

Additionally, polynucleotides, polypeptides, and/or agonists or antagonists of the invention may affect apoptosis, and therefore, would be useful in treating a number of diseases associated with increased cell survival or the inhibition of apoptosis. For example, diseases associated with increased cell survival or the inhibition of apoptosis that could be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated by polynucleotides, polypeptides, and/or agonists or antagonists of the invention, include cancers (such as follicular lymphomas, carcinomas with p53 mutations, and hormone-dependent tumors, including, but not limited to colon cancer, cardiac tumors, pancreatic cancer, melanoma, retinoblastoma, glioblastoma, lung cancer, intestinal cancer, testicular cancer, stomach cancer, neuroblastoma, myxoma, myoma, lymphoma, endothelioma, osteoblastoma, osteoclastoma, osteosarcoma, chondrosarcoma, adenoma, breast cancer, prostate cancer, Kaposi's sarcoma and ovarian cancer); autoimmune disorders such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) and viral infections (such as herpes viruses, pox viruses and adenoviruses), inflammation, graft v. host disease, acute graft rejection, and chronic graft rejection.

In preferred embodiments, polynucleotides, polypeptides, and/or agonists or antagonists of the invention are used to inhibit growth, progression, and/or metastasis of cancers, in particular those listed above.

Additional diseases or conditions associated with increased cell survival that could be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated by polynucleotides, polypeptides, and/or agonists or antagonists of the invention, include, but are not limited to, progression, and/or metastases of malignancies and related disorders such as leukemia (including acute leukemias (e.g., acute lymphocytic leukemia, acute myelocytic leukemia (including

myeloblastic, promyelocytic, myelomonocytic, monocytic, and erythroleukemia)) and chronic leukemias (e.g., chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia)), polycythemia vera, lymphomas (e.g., Hodgkin's disease and non-Hodgkin's disease), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, and solid tumors including, but
 5 not limited to, sarcomas and carcinomas such as fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat
 10 gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma,
 15 pinealoma, emangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, melanoma, neuroblastoma, and retinoblastoma.

Diseases associated with increased apoptosis that could be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated by polynucleotides, polypeptides, and/or agonists or antagonists of the invention, include AIDS; neurodegenerative disorders (such as Alzheimer's
 20 disease, Parkinson's disease, amyotrophic lateral sclerosis, retinitis pigmentosa, cerebellar degeneration and brain tumor or prior associated disease); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) myelodysplastic syndromes (such as aplastic anemia),
 25 graft v. host disease, ischemic injury (such as that caused by myocardial infarction, stroke and reperfusion injury), liver injury (e.g., hepatitis related liver injury, ischemia/reperfusion injury, cholestasis (bile duct injury) and liver cancer); toxin-induced liver disease (such as that caused by alcohol), septic shock, cachexia and anorexia.

Hyperproliferative diseases and/or disorders that could be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated by polynucleotides, polypeptides, and/or agonists or
 30 antagonists of the invention, include, but are not limited to, neoplasms located in the liver, abdomen, bone, breast, digestive system, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous system (central and peripheral), lymphatic system, pelvis, skin, soft tissue, spleen, thorax, and urogenital
 35 tract.

Similarly, other hyperproliferative disorders can also be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated by polynucleotides, polypeptides, and/or agonists or

antagonists of the invention. Examples of such hyperproliferative disorders include, but are not limited to: hypergammaglobulinemia, lymphoproliferative disorders, paraproteinemias, purpura, sarcoidosis, Sezary Syndrome, Waldenstrom's macroglobulinemia, Gaucher's Disease, histiocytosis, and any other hyperproliferative disease, besides neoplasia, located in an organ
5 system listed above.

Another preferred embodiment utilizes polynucleotides of the present invention to inhibit aberrant cellular division, by gene therapy using the present invention, and/or protein fusions or fragments thereof.

Thus, the present invention provides a method for treating cell proliferative disorders by
10 inserting into an abnormally proliferating cell a polynucleotide of the present invention, wherein said polynucleotide represses said expression.

Another embodiment of the present invention provides a method of treating cell-proliferative disorders in individuals comprising administration of one or more active gene copies of the present invention to an abnormally proliferating cell or cells. In a preferred embodiment,
15 polynucleotides of the present invention is a DNA construct comprising a recombinant expression vector effective in expressing a DNA sequence encoding said polynucleotides. In another preferred embodiment of the present invention, the DNA construct encoding the polynucleotides of the present invention is inserted into cells to be treated utilizing a retrovirus, or more preferably an adenoviral vector (See G J. Nabel, et. al., PNAS 1999 96: 324-326, which is hereby incorporated
20 by reference). In a most preferred embodiment, the viral vector is defective and will not transform non-proliferating cells, only proliferating cells. Moreover, in a preferred embodiment, the polynucleotides of the present invention inserted into proliferating cells either alone, or in combination with or fused to other polynucleotides, can then be modulated via an external stimulus (i.e. magnetic, specific small molecule, chemical, or drug administration, etc.), which acts
25 upon the promoter upstream of said polynucleotides to induce expression of the encoded protein product. As such the beneficial therapeutic affect of the present invention may be expressly modulated (i.e. to increase, decrease, or inhibit expression of the present invention) based upon said external stimulus.

Polynucleotides of the present invention may be useful in repressing expression of
30 oncogenic genes or antigens. By "repressing expression of the oncogenic genes " is intended the suppression of the transcription of the gene, the degradation of the gene transcript (pre-message RNA), the inhibition of splicing, the destruction of the messenger RNA, the prevention of the post-translational modifications of the protein, the destruction of the protein, or the inhibition of the normal function of the protein.

35 For local administration to abnormally proliferating cells, polynucleotides of the present invention may be administered by any method known to those of skill in the art including, but not limited to transfection, electroporation, microinjection of cells, or in vehicles such as liposomes,

lipofectin, or as naked polynucleotides, or any other method described throughout the specification. The polynucleotide of the present invention may be delivered by known gene delivery systems such as, but not limited to, retroviral vectors (Gilboa, J. Virology 44:845 (1982); Hocke, Nature 320:275 (1986); Wilson, et al., Proc. Natl. Acad. Sci. U.S.A. 85:3014), vaccinia virus system (Chakrabarty et al., Mol. Cell Biol. 5:3403 (1985) or other efficient DNA delivery systems (Yates et al., Nature 313:812 (1985)) known to those skilled in the art. These references are exemplary only and are hereby incorporated by reference. In order to specifically deliver or transfect cells which are abnormally proliferating and spare non-dividing cells, it is preferable to utilize a retrovirus, or adenoviral (as described in the art and elsewhere herein) delivery system known to those of skill in the art. Since host DNA replication is required for retroviral DNA to integrate and the retrovirus will be unable to self replicate due to the lack of the retrovirus genes needed for its life cycle. Utilizing such a retroviral delivery system for polynucleotides of the present invention will target said gene and constructs to abnormally proliferating cells and will spare the non-dividing normal cells.

The polynucleotides of the present invention may be delivered directly to cell proliferative disorder/disease sites in internal organs, body cavities and the like by use of imaging devices used to guide an injecting needle directly to the disease site. The polynucleotides of the present invention may also be administered to disease sites at the time of surgical intervention.

By "cell proliferative disease" is meant any human or animal disease or disorder, affecting any one or any combination of organs, cavities, or body parts, which is characterized by single or multiple local abnormal proliferations of cells, groups of cells, or tissues, whether benign or malignant.

Any amount of the polynucleotides of the present invention may be administered as long as it has a biologically inhibiting effect on the proliferation of the treated cells. Moreover, it is possible to administer more than one of the polynucleotide of the present invention simultaneously to the same site. By "biologically inhibiting" is meant partial or total growth inhibition as well as decreases in the rate of proliferation or growth of the cells. The biologically inhibitory dose may be determined by assessing the effects of the polynucleotides of the present invention on target malignant or abnormally proliferating cell growth in tissue culture, tumor growth in animals and cell cultures, or any other method known to one of ordinary skill in the art.

The present invention is further directed to antibody-based therapies which involve administering of anti-polypeptides and anti-polynucleotide antibodies to a mammalian, preferably human, patient for treating one or more of the described disorders. Methods for producing anti-polypeptides and anti-polynucleotide antibodies polyclonal and monoclonal antibodies are described in detail elsewhere herein. Such antibodies may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

A summary of the ways in which the antibodies of the present invention may be used therapeutically includes binding polynucleotides or polypeptides of the present invention locally or systemically in the body or by direct cytotoxicity of the antibody, e.g. as mediated by complement (CDC) or by effector cells (ADCC). Some of these approaches are described in more detail below.

5 Armed with the teachings provided herein, one of ordinary skill in the art will know how to use the antibodies of the present invention for diagnosis, prognosis, monitoring, or therapeutic purposes without undue experimentation.

In particular, the antibodies, fragments and derivatives of the present invention are useful for treating a subject having or developing cell proliferative and/or differentiation disorders as

10 described herein. Such treatment comprises administering a single or multiple doses of the antibody, or a fragment, derivative, or a conjugate thereof.

The antibodies of this invention may be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors, for example., which serve to increase the number or activity of effector cells which interact with the

15 antibodies.

It is preferred to use high affinity and/or potent *in vivo* inhibiting and/or neutralizing antibodies against polypeptides or polynucleotides of the present invention, fragments or regions thereof, for both immunoassays directed to and therapy of disorders related to polynucleotides or polypeptides, including fragments thereof, of the present invention. Such antibodies, fragments,

20 or regions, will preferably have an affinity for polynucleotides or polypeptides, including fragments thereof. Preferred binding affinities include those with a dissociation constant or K_d less than $5 \times 10^{-6}M$, $10^{-6}M$, $5 \times 10^{-7}M$, $10^{-7}M$, $5 \times 10^{-8}M$, $10^{-8}M$, $5 \times 10^{-9}M$, $10^{-9}M$, $5 \times 10^{-10}M$, $10^{-10}M$, $5 \times 10^{-11}M$, $10^{-11}M$, $5 \times 10^{-12}M$, $10^{-12}M$, $5 \times 10^{-13}M$, $10^{-13}M$, $5 \times 10^{-14}M$, $10^{-14}M$, $5 \times 10^{-15}M$, and $10^{-15}M$.

Moreover, polypeptides of the present invention are useful in inhibiting the angiogenesis of proliferative cells or tissues, either alone, as a protein fusion, or in combination with other polypeptides directly or indirectly, as described elsewhere herein. In a most preferred embodiment, said anti-angiogenesis effect may be achieved indirectly, for example, through the inhibition of hematopoietic, tumor-specific cells, such as tumor-associated macrophages (See Joseph IB, et al. J

30 Natl Cancer Inst, 90(21):1648-53 (1998), which is hereby incorporated by reference). Antibodies directed to polypeptides or polynucleotides of the present invention may also result in inhibition of angiogenesis directly, or indirectly (See Witte L, et al., Cancer Metastasis Rev. 17(2):155-61 (1998), which is hereby incorporated by reference)).

Polypeptides, including protein fusions, of the present invention, or fragments thereof may

35 be useful in inhibiting proliferative cells or tissues through the induction of apoptosis. Said polypeptides may act either directly, or indirectly to induce apoptosis of proliferative cells and tissues, for example in the activation of a death-domain receptor, such as tumor necrosis factor

(TNF) receptor-1, CD95 (Fas/APO-1), TNF-receptor-related apoptosis-mediated protein (TRAMP) and TNF-related apoptosis-inducing ligand (TRAIL) receptor-1 and -2 (See Schulze-Osthoff K, et.al., Eur J Biochem 254(3):439-59 (1998), which is hereby incorporated by reference). Moreover, in another preferred embodiment of the present invention, said polypeptides
5 may induce apoptosis through other mechanisms, such as in the activation of other proteins which will activate apoptosis, or through stimulating the expression of said proteins, either alone or in combination with small molecule drugs or adjuvants, such as apoptonin, galectins, thioredoxins, anti-inflammatory proteins (See for example, Mutat Res 400(1-2):447-55 (1998), Med Hypotheses.50(5):423-33 (1998), Chem Biol Interact. Apr 24;111-112:23-34 (1998), J Mol
10 Med.76(6):402-12 (1998), Int J Tissue React;20(1):3-15 (1998), which are all hereby incorporated by reference).

Polypeptides, including protein fusions to, or fragments thereof, of the present invention are useful in inhibiting the metastasis of proliferative cells or tissues. Inhibition may occur as a direct result of administering polypeptides, or antibodies directed to said polypeptides as described
15 elsewhere herein, or indirectly, such as activating the expression of proteins known to inhibit metastasis, for example alpha 4 integrins, (See, e.g., Curr Top Microbiol Immunol 1998;231:125-41, which is hereby incorporated by reference). Such therapeutic affects of the present invention may be achieved either alone, or in combination with small molecule drugs or adjuvants.

In another embodiment, the invention provides a method of delivering compositions
20 containing the polypeptides of the invention (e.g., compositions containing polypeptides or polypeptide antibodies associated with heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs) to targeted cells expressing the polypeptide of the present invention. Polypeptides or polypeptide antibodies of the invention may be associated with with heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs via hydrophobic, hydrophilic, ionic
25 and/or covalent interactions.

Polypeptides, protein fusions to, or fragments thereof, of the present invention are useful in enhancing the immunogenicity and/or antigenicity of proliferating cells or tissues, either directly, such as would occur if the polypeptides of the present invention 'vaccinated' the immune response to respond to proliferative antigens and immunogens, or indirectly, such as in activating
30 the expression of proteins known to enhance the immune response (e.g. chemokines), to said antigens and immunogens.

Anti-Angiogenesis Activity

The naturally occurring balance between endogenous stimulators and inhibitors of
35 angiogenesis is one in which inhibitory influences predominate. Rastinejad *et al.*, *Cell* 56:345-355 (1989). In those rare instances in which neovascularization occurs under normal physiological conditions, such as wound healing, organ regeneration, embryonic development, and female

reproductive processes, angiogenesis is stringently regulated and spatially and temporally delimited. Under conditions of pathological angiogenesis such as that characterizing solid tumor growth, these regulatory controls fail. Unregulated angiogenesis becomes pathologic and sustains progression of many neoplastic and non-neoplastic diseases. A number of serious diseases are dominated by abnormal neovascularization including solid tumor growth and metastases, arthritis, some types of eye disorders, and psoriasis. See, e.g., reviews by Moses *et al.*, *Biotech.* 9:630-634 (1991); Folkman *et al.*, *N. Engl. J. Med.*, 333:1757-1763 (1995); Auerbach *et al.*, *J. Microvasc. Res.* 29:401-411 (1985); Folkman, *Advances in Cancer Research*, eds. Klein and Weinhouse, Academic Press, New York, pp. 175-203 (1985); Patz, *Am. J. Ophthalmol.* 94:715-743 (1982); and Folkman *et al.*, *Science* 221:719-725 (1983). In a number of pathological conditions, the process of angiogenesis contributes to the disease state. For example, significant data have accumulated which suggest that the growth of solid tumors is dependent on angiogenesis. Folkman and Klagsbrun, *Science* 235:442-447 (1987).

The present invention provides for treatment of diseases or disorders associated with neovascularization by administration of the polynucleotides and/or polypeptides of the invention, as well as agonists or antagonists of the present invention. Malignant and metastatic conditions which can be treated with the polynucleotides and polypeptides, or agonists or antagonists of the invention include, but are not limited to, malignancies, solid tumors, and cancers described herein and otherwise known in the art (for a review of such disorders, see Fishman *et al.*, *Medicine*, 2d Ed., J. B. Lippincott Co., Philadelphia (1985)). Thus, the present invention provides a method of treating an angiogenesis-related disease and/or disorder, comprising administering to an individual in need thereof a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist of the invention. For example, polynucleotides, polypeptides, antagonists and/or agonists may be utilized in a variety of additional methods in order to therapeutically treat a cancer or tumor. Cancers which may be treated with polynucleotides, polypeptides, antagonists and/or agonists include, but are not limited to solid tumors, including prostate, lung, breast, ovarian, stomach, pancreas, larynx, esophagus, testes, liver, parotid, biliary tract, colon, rectum, cervix, uterus, endometrium, kidney, bladder, thyroid cancer; primary tumors and metastases; melanomas; glioblastoma; Kaposi's sarcoma; leiomyosarcoma; non-small cell lung cancer; colorectal cancer; advanced malignancies; and blood born tumors such as leukemias. For example, polynucleotides, polypeptides, antagonists and/or agonists may be delivered topically, in order to treat cancers such as skin cancer, head and neck tumors, breast tumors, and Kaposi's sarcoma.

Within yet other aspects, polynucleotides, polypeptides, antagonists and/or agonists may be utilized to treat superficial forms of bladder cancer by, for example, intravesical administration. Polynucleotides, polypeptides, antagonists and/or agonists may be delivered directly into the tumor, or near the tumor site, via injection or a catheter. Of course, as the artisan of ordinary skill will appreciate, the appropriate mode of administration will vary according to the cancer to be

treated. Other modes of delivery are discussed herein.

Polynucleotides, polypeptides, antagonists and/or agonists may be useful in treating other disorders, besides cancers, which involve angiogenesis. These disorders include, but are not limited to: benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; arteriosclerotic plaques; ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uveitis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid arthritis; psoriasis; delayed wound healing; endometriosis; vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque neovascularization; telangiectasia; hemophilic joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis.

For example, within one aspect of the present invention methods are provided for treating hypertrophic scars and keloids, comprising the step of administering a polynucleotide, polypeptide, antagonist and/or agonist of the invention to a hypertrophic scar or keloid.

Within one embodiment of the present invention polynucleotides, polypeptides, antagonists and/or agonists of the invention are directly injected into a hypertrophic scar or keloid, in order to prevent the progression of these lesions. This therapy is of particular value in the prophylactic treatment of conditions which are known to result in the development of hypertrophic scars and keloids (e.g., burns), and is preferably initiated after the proliferative phase has had time to progress (approximately 14 days after the initial injury), but before hypertrophic scar or keloid development. As noted above, the present invention also provides methods for treating neovascular diseases of the eye, including for example, corneal neovascularization, neovascular glaucoma, proliferative diabetic retinopathy, retrolental fibroplasia and macular degeneration.

Moreover, Ocular disorders associated with neovascularization which can be treated with the polynucleotides and polypeptides of the present invention (including agonists and/or antagonists) include, but are not limited to: neovascular glaucoma, diabetic retinopathy, retinoblastoma, retrolental fibroplasia, uveitis, retinopathy of prematurity macular degeneration, corneal graft neovascularization, as well as other eye inflammatory diseases, ocular tumors and diseases associated with choroidal or iris neovascularization. See, e.g., reviews by Waltman *et al.*, *Am. J. Ophthalmol.* 85:704-710 (1978) and Gartner *et al.*, *Surv. Ophthalmol.* 22:291-312 (1978).

Thus, within one aspect of the present invention methods are provided for treating neovascular diseases of the eye such as corneal neovascularization (including corneal graft neovascularization), comprising the step of administering to a patient a therapeutically effective amount of a compound (as described above) to the cornea, such that the formation of blood vessels is inhibited. Briefly, the cornea is a tissue which normally lacks blood vessels. In certain

pathological conditions however, capillaries may extend into the cornea from the pericorneal vascular plexus of the limbus. When the cornea becomes vascularized, it also becomes clouded, resulting in a decline in the patient's visual acuity. Visual loss may become complete if the cornea completely opacitates. A wide variety of disorders can result in corneal neovascularization, including for example, corneal infections (e.g., trachoma, herpes simplex keratitis, leishmaniasis and onchocerciasis), immunological processes (e.g., graft rejection and Stevens-Johnson's syndrome), alkali burns, trauma, inflammation (of any cause), toxic and nutritional deficiency states, and as a complication of wearing contact lenses.

Within particularly preferred embodiments of the invention, may be prepared for topical administration in saline (combined with any of the preservatives and antimicrobial agents commonly used in ocular preparations), and administered in eyedrop form. The solution or suspension may be prepared in its pure form and administered several times daily. Alternatively, anti-angiogenic compositions, prepared as described above, may also be administered directly to the cornea. Within preferred embodiments, the anti-angiogenic composition is prepared with a muco-adhesive polymer which binds to cornea. Within further embodiments, the anti-angiogenic factors or anti-angiogenic compositions may be utilized as an adjunct to conventional steroid therapy. Topical therapy may also be useful prophylactically in corneal lesions which are known to have a high probability of inducing an angiogenic response (such as chemical burns). In these instances the treatment, likely in combination with steroids, may be instituted immediately to help prevent subsequent complications.

Within other embodiments, the compounds described above may be injected directly into the corneal stroma by an ophthalmologist under microscopic guidance. The preferred site of injection may vary with the morphology of the individual lesion, but the goal of the administration would be to place the composition at the advancing front of the vasculature (i.e., interspersed between the blood vessels and the normal cornea). In most cases this would involve perilimbal corneal injection to "protect" the cornea from the advancing blood vessels. This method may also be utilized shortly after a corneal insult in order to prophylactically prevent corneal neovascularization. In this situation the material could be injected in the perilimbal cornea interspersed between the corneal lesion and its undesired potential limbal blood supply. Such methods may also be utilized in a similar fashion to prevent capillary invasion of transplanted corneas. In a sustained-release form injections might only be required 2-3 times per year. A steroid could also be added to the injection solution to reduce inflammation resulting from the injection itself.

Within another aspect of the present invention, methods are provided for treating neovascular glaucoma, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eye, such that the formation of blood vessels is inhibited. In one embodiment, the compound may be administered

topically to the eye in order to treat early forms of neovascular glaucoma. Within other embodiments, the compound may be implanted by injection into the region of the anterior chamber angle. Within other embodiments, the compound may also be placed in any location such that the compound is continuously released into the aqueous humor. Within another aspect of the present invention, methods are provided for treating proliferative diabetic retinopathy, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eyes, such that the formation of blood vessels is inhibited.

Within particularly preferred embodiments of the invention, proliferative diabetic retinopathy may be treated by injection into the aqueous humor or the vitreous, in order to increase the local concentration of the polynucleotide, polypeptide, antagonist and/or agonist in the retina. Preferably, this treatment should be initiated prior to the acquisition of severe disease requiring photocoagulation.

Within another aspect of the present invention, methods are provided for treating retrolental fibroplasia, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eye, such that the formation of blood vessels is inhibited. The compound may be administered topically, via intravitreal injection and/or via intraocular implants.

Additionally, disorders which can be treated with the polynucleotides, polypeptides, agonists and/or antagonists include, but are not limited to, hemangioma, arthritis, psoriasis, angiofibroma, atherosclerotic plaques, delayed wound healing, granulations, hemophilic joints, hypertrophic scars, nonunion fractures, Osler-Weber syndrome, pyogenic granuloma, scleroderma, trachoma, and vascular adhesions.

Moreover, disorders and/or states, which can be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated with the the polynucleotides, polypeptides, agonists and/or antagonists of the invention include, but are not limited to, solid tumors, blood born tumors such as leukemias, tumor metastasis, Kaposi's sarcoma, benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas, rheumatoid arthritis, psoriasis, ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, and uveitis, delayed wound healing, endometriosis, vasculogenesis, granulations, hypertrophic scars (keloids), nonunion fractures, scleroderma, trachoma, vascular adhesions, myocardial angiogenesis, coronary collaterals, cerebral collaterals, arteriovenous malformations, ischemic limb angiogenesis, Osler-Webber Syndrome, plaque neovascularization, telangiectasia, hemophilic joints, angiofibroma fibromuscular dysplasia, wound granulation, Crohn's disease, atherosclerosis, birth control agent by preventing vascularization required for embryo implantation controlling menstruation, diseases that have

angiogenesis as a pathologic consequence such as cat scratch disease (*Rochela minalia quintosa*), ulcers (*Helicobacter pylori*), Bartonellosis and bacillary angiomatosis.

In one aspect of the birth control method, an amount of the compound sufficient to block embryo implantation is administered before or after intercourse and fertilization have occurred, thus providing an effective method of birth control, possibly a "morning after" method. Polynucleotides, polypeptides, agonists and/or agonists may also be used in controlling menstruation or administered as either a peritoneal lavage fluid or for peritoneal implantation in the treatment of endometriosis.

Polynucleotides, polypeptides, agonists and/or agonists of the present invention may be incorporated into surgical sutures in order to prevent stitch granulomas.

Polynucleotides, polypeptides, agonists and/or agonists may be utilized in a wide variety of surgical procedures. For example, within one aspect of the present invention a compositions (in the form of, for example, a spray or film) may be utilized to coat or spray an area prior to removal of a tumor, in order to isolate normal surrounding tissues from malignant tissue, and/or to prevent the spread of disease to surrounding tissues. Within other aspects of the present invention, compositions (e.g., in the form of a spray) may be delivered via endoscopic procedures in order to coat tumors, or inhibit angiogenesis in a desired locale. Within yet other aspects of the present invention, surgical meshes which have been coated with anti-angiogenic compositions of the present invention may be utilized in any procedure wherein a surgical mesh might be utilized. For example, within one embodiment of the invention a surgical mesh laden with an anti-angiogenic composition may be utilized during abdominal cancer resection surgery (e.g., subsequent to colon resection) in order to provide support to the structure, and to release an amount of the anti-angiogenic factor.

Within further aspects of the present invention, methods are provided for treating tumor excision sites, comprising administering a polynucleotide, polypeptide, agonist and/or agonist to the resection margins of a tumor subsequent to excision, such that the local recurrence of cancer and the formation of new blood vessels at the site is inhibited. Within one embodiment of the invention, the anti-angiogenic compound is administered directly to the tumor excision site (e.g., applied by swabbing, brushing or otherwise coating the resection margins of the tumor with the anti-angiogenic compound). Alternatively, the anti-angiogenic compounds may be incorporated into known surgical pastes prior to administration. Within particularly preferred embodiments of the invention, the anti-angiogenic compounds are applied after hepatic resections for malignancy, and after neurosurgical operations.

Within one aspect of the present invention, polynucleotides, polypeptides, agonists and/or agonists may be administered to the resection margin of a wide variety of tumors, including for example, breast, colon, brain and hepatic tumors. For example, within one embodiment of the

invention, anti-angiogenic compounds may be administered to the site of a neurological tumor subsequent to excision, such that the formation of new blood vessels at the site are inhibited.

The polynucleotides, polypeptides, agonists and/or agonists of the present invention may also be administered along with other anti-angiogenic factors. Representative examples of other anti-angiogenic factors include: Anti-Invasive Factor, retinoic acid and derivatives thereof, paclitaxel, Suramin, Tissue Inhibitor of Metalloproteinase-1, Tissue Inhibitor of Metalloproteinase-2, Plasminogen Activator Inhibitor-1, Plasminogen Activator Inhibitor-2, and various forms of the lighter "d group" transition metals.

Lighter "d group" transition metals include, for example, vanadium, molybdenum, tungsten, titanium, niobium, and tantalum species. Such transition metal species may form transition metal complexes. Suitable complexes of the above-mentioned transition metal species include oxo transition metal complexes.

Representative examples of vanadium complexes include oxo vanadium complexes such as vanadate and vanadyl complexes. Suitable vanadate complexes include metavanadate and orthovanadate complexes such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates.

Representative examples of tungsten and molybdenum complexes also include oxo complexes. Suitable oxo tungsten complexes include tungstate and tungsten oxide complexes. Suitable tungstate complexes include ammonium tungstate, calcium tungstate, sodium tungstate dihydrate, and tungstic acid. Suitable tungsten oxides include tungsten (IV) oxide and tungsten (VI) oxide. Suitable oxo molybdenum complexes include molybdate, molybdenum oxide, and molybdenyl complexes. Suitable molybdate complexes include ammonium molybdate and its hydrates, sodium molybdate and its hydrates, and potassium molybdate and its hydrates. Suitable molybdenum oxides include molybdenum (VI) oxide, molybdenum (VI) oxide, and molybdic acid. Suitable molybdenyl complexes include, for example, molybdenyl acetylacetonate. Other suitable tungsten and molybdenum complexes include hydroxo derivatives derived from, for example, glycerol, tartaric acid, and sugars.

A wide variety of other anti-angiogenic factors may also be utilized within the context of the present invention. Representative examples include platelet factor 4; protamine sulphate; sulphated chitin derivatives (prepared from queen crab shells), (Murata et al., Cancer Res. 51:22-26, 1991); Sulphated Polysaccharide Peptidoglycan Complex (SP- PG) (the function of this compound may be enhanced by the presence of steroids such as estrogen, and tamoxifen citrate); Staurosporine; modulators of matrix metabolism, including for example, proline analogs, cis-hydroxyproline, d,L-3,4-dehydroproline, Thiaproline, alpha,alpha-dipyridyl, aminopropionitrile fumarate; 4-propyl-5-(4-pyridinyl)-2(3H)-oxazolone; Methotrexate; Mitoxantrone; Heparin;

Interferons; 2 Macroglobulin-serum; ChIMP-3 (Pavloff et al., J. Bio. Chem. 267:17321-17326, 1992); Chymostatin (Tomkinson et al., Biochem J. 286:475-480, 1992); Cyclodextrin Tetradasulfate; Eponemycin; Camptothecin; Fumagillin (Ingber et al., Nature 348:555-557, 1990); Gold Sodium Thiomalate ("GST"; Matsubara and Ziff, J. Clin. Invest. 79:1440-1446, 5 1987); anticollagenase-serum; alpha2-antiplasmin (Holmes et al., J. Biol. Chem. 262(4):1659-1664, 1987); Bisantrene (National Cancer Institute); Lobenzarit disodium (N-(2)-carboxyphenyl-4-chloroanthronilic acid disodium or "CCA"; Takeuchi et al., Agents Actions 36:312-316, 1992); Thalidomide; Angostatic steroid; AGM-1470; carboxynaminolmidazole; and metalloproteinase inhibitors such as BB94.

10

Diseases at the Cellular Level

Diseases associated with increased cell survival or the inhibition of apoptosis that could be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated using polynucleotides or polypeptides, as well as antagonists or agonists of the present invention, include cancers (such 15 as follicular lymphomas, carcinomas with p53 mutations, and hormone-dependent tumors, including, but not limited to colon cancer, cardiac tumors, pancreatic cancer, melanoma, retinoblastoma, glioblastoma, lung cancer, intestinal cancer, testicular cancer, stomach cancer, neuroblastoma, myxoma, myoma, lymphoma, endothelioma, osteoblastoma, osteoclastoma, osteosarcoma, chondrosarcoma, adenoma, breast cancer, prostate cancer, Kaposi's sarcoma and 20 ovarian cancer); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) and viral infections (such as herpes viruses, pox viruses and adenoviruses), inflammation, graft v. host disease, acute graft rejection, and chronic graft rejection.

25 In preferred embodiments, polynucleotides, polypeptides, and/or antagonists of the invention are used to inhibit growth, progression, and/or metasis of cancers, in particular those listed above.

Additional diseases or conditions associated with increased cell survival that could be treated or detected by polynucleotides or polypeptides, or agonists or antagonists of the present 30 invention include, but are not limited to, progression, and/or metastases of malignancies and related disorders such as leukemia (including acute leukemias (e.g., acute lymphocytic leukemia, acute myelocytic leukemia (including myeloblastic, promyelocytic, myelomonocytic, monocytic, and erythroleukemia)) and chronic leukemias (e.g., chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia)), polycythemia vera, lymphomas (e.g., Hodgkin's disease and 35 non-Hodgkin's disease), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, and solid tumors including, but not limited to, sarcomas and carcinomas such as fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma,

angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, melanoma, neuroblastoma, and retinoblastoma.

Diseases associated with increased apoptosis that could be detected, prevented, diagnosed, prognosticated, treated, and/or ameliorated using polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, include, but are not limited to, AIDS; neurodegenerative disorders (such as Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis, Retinitis pigmentosa, Cerebellar degeneration and brain tumor or prior associated disease); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) myelodysplastic syndromes (such as aplastic anemia), graft v. host disease, ischemic injury (such as that caused by myocardial infarction, stroke and reperfusion injury), liver injury (e.g., hepatitis related liver injury, ischemia/reperfusion injury, cholestasis (bile duct injury) and liver cancer); toxin-induced liver disease (such as that caused by alcohol), septic shock, cachexia and anorexia.

25 Wound Healing and Epithelial Cell Proliferation

In accordance with yet a further aspect of the present invention, there is provided a process for utilizing polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, for therapeutic purposes, for example, to stimulate epithelial cell proliferation and basal keratinocytes for the purpose of wound healing, and to stimulate hair follicle production and healing of dermal wounds. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may be clinically useful in stimulating wound healing including surgical wounds, excisional wounds, deep wounds involving damage of the dermis and epidermis, eye tissue wounds, dental tissue wounds, oral cavity wounds, diabetic ulcers, dermal ulcers, cubitus ulcers, arterial ulcers, venous stasis ulcers, burns resulting from heat exposure or chemicals, and other abnormal wound healing conditions such as uremia, malnutrition, vitamin deficiencies and complications associated with systemic treatment with steroids, radiation therapy and antineoplastic drugs and antimetabolites. Polynucleotides or polypeptides, as well as agonists or

antagonists of the present invention, could be used to promote dermal reestablishment subsequent to dermal loss

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to increase the adherence of skin grafts to a wound bed and to stimulate re-epithelialization from the wound bed. The following are types of grafts that polynucleotides or polypeptides, agonists or antagonists of the present invention, could be used to increase adherence to a wound bed: autografts, artificial skin, allografts, autodermic graft, autoepidermic grafts, avascular grafts, Blair-Brown grafts, bone graft, brephoplastic grafts, cutis graft, delayed graft, dermic graft, epidermic graft, fascia graft, full thickness graft, heterologous graft, xenograft, homologous graft, hyperplastic graft, lamellar graft, mesh graft, mucosal graft, Ollier-Thiersch graft, omentopial graft, patch graft, pedicle graft, penetrating graft, split skin graft, thick split graft. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, can be used to promote skin strength and to improve the appearance of aged skin.

It is believed that polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, will also produce changes in hepatocyte proliferation, and epithelial cell proliferation in the lung, breast, pancreas, stomach, small intestine, and large intestine. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could promote proliferation of epithelial cells such as sebocytes, hair follicles, hepatocytes, type II pneumocytes, mucin-producing goblet cells, and other epithelial cells and their progenitors contained within the skin, lung, liver, and gastrointestinal tract. Polynucleotides or polypeptides, agonists or antagonists of the present invention, may promote proliferation of endothelial cells, keratinocytes, and basal keratinocytes.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could also be used to reduce the side effects of gut toxicity that result from radiation, chemotherapy treatments or viral infections. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may have a cytoprotective effect on the small intestine mucosa. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may also stimulate healing of mucositis (mouth ulcers) that result from chemotherapy and viral infections.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could further be used in full regeneration of skin in full and partial thickness skin defects, including burns, (i.e., repopulation of hair follicles, sweat glands, and sebaceous glands), treatment of other skin defects such as psoriasis. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat epidermolysis bullosa, a defect in adherence of the epidermis to the underlying dermis which results in frequent, open and painful blisters by accelerating reepithelialization of these lesions. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could also be used to treat

gastric and duodenal ulcers and help heal by scar formation of the mucosal lining and regeneration of glandular mucosa and duodenal mucosal lining more rapidly. Inflammatory bowel diseases, such as Crohn's disease and ulcerative colitis, are diseases which result in destruction of the mucosal surface of the small or large intestine, respectively. Thus, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to promote the resurfacing of the mucosal surface to aid more rapid healing and to prevent progression of inflammatory bowel disease. Treatment with polynucleotides or polypeptides, agonists or antagonists of the present invention, is expected to have a significant effect on the production of mucus throughout the gastrointestinal tract and could be used to protect the intestinal mucosa from injurious substances that are ingested or following surgery. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat diseases associated with the under expression.

Moreover, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to prevent and heal damage to the lungs due to various pathological states. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, which could stimulate proliferation and differentiation and promote the repair of alveoli and bronchiolar epithelium to prevent or treat acute or chronic lung damage. For example, emphysema, which results in the progressive loss of alveoli, and inhalation injuries, i.e., resulting from smoke inhalation and burns, that cause necrosis of the bronchiolar epithelium and alveoli could be effectively treated using polynucleotides or polypeptides, agonists or antagonists of the present invention. Also, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to stimulate the proliferation of and differentiation of type II pneumocytes, which may help treat or prevent disease such as hyaline membrane diseases, such as infant respiratory distress syndrome and bronchopulmonary dysplasia, in premature infants.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could stimulate the proliferation and differentiation of hepatocytes and, thus, could be used to alleviate or treat liver diseases and pathologies such as fulminant liver failure caused by cirrhosis, liver damage caused by viral hepatitis and toxic substances (i.e., acetaminophen, carbon tetrachloride and other hepatotoxins known in the art).

In addition, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat or prevent the onset of diabetes mellitus. In patients with newly diagnosed Types I and II diabetes, where some islet cell function remains, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to maintain the islet function so as to alleviate, delay or prevent permanent manifestation of the disease. Also, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used as an auxiliary in islet cell transplantation to improve or promote islet cell function.

Regeneration

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention can be used to differentiate, proliferate, and attract cells, leading to the regeneration of tissues. (See, Science 276:59-87 (1997)). The regeneration of tissues could be used to repair, replace, or
5 protect tissue damaged by congenital defects, trauma (wounds, burns, incisions, or ulcers), age, disease (e.g. osteoporosis, osteoarthritis, periodontal disease, liver failure), surgery, including cosmetic plastic surgery, fibrosis, reperfusion injury, or systemic cytokine damage.

Tissues that could be regenerated using the present invention include organs (e.g., pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac),
10 vasculature (including vascular and lymphatics), nervous, hematopoietic, and skeletal (bone, cartilage, tendon, and ligament) tissue. Preferably, regeneration occurs without or decreased scarring. Regeneration also may include angiogenesis.

Moreover, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may increase regeneration of tissues difficult to heal. For example, increased
15 tendon/ligament regeneration would quicken recovery time after damage. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention could also be used prophylactically in an effort to avoid damage. Specific diseases that could be treated include of tendinitis, carpal tunnel syndrome, and other tendon or ligament defects. A further example of tissue regeneration of non-healing wounds includes pressure ulcers, ulcers associated with vascular
20 insufficiency, surgical, and traumatic wounds.

Similarly, nerve and brain tissue could also be regenerated by using polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, to proliferate and differentiate nerve cells. Diseases that could be treated using this method include central and peripheral nervous system diseases, neuropathies, or mechanical and traumatic disorders (e.g.,
25 spinal cord disorders, head trauma, cerebrovascular disease, and stroke). Specifically, diseases associated with peripheral nerve injuries, peripheral neuropathy (e.g., resulting from chemotherapy or other medical therapies), localized neuropathies, and central nervous system diseases (e.g., Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome), could all be treated using the polynucleotides or polypeptides, as well as
30 agonists or antagonists of the present invention.

Chemotaxis

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may have chemotaxis activity. A chemotactic molecule attracts or mobilizes cells (e.g.,
35 monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells) to a particular site in the body, such as inflammation, infection, or site of hyperproliferation. The mobilized cells can then fight off and/or heal the particular trauma or abnormality.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may increase chemotactic activity of particular cells. These chemotactic molecules can then be used to treat inflammation, infection, hyperproliferative disorders, or any immune system disorder by increasing the number of cells targeted to a particular location in the body. For example, chemotactic molecules can be used to treat wounds and other trauma to tissues by attracting immune cells to the injured location. Chemotactic molecules of the present invention can also attract fibroblasts, which can be used to treat wounds.

It is also contemplated that polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may inhibit chemotactic activity. These molecules could also be used to treat disorders. Thus, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention could be used as an inhibitor of chemotaxis.

Binding Activity

A polypeptide of the present invention may be used to screen for molecules that bind to the polypeptide or for molecules to which the polypeptide binds. The binding of the polypeptide and the molecule may activate (agonist), increase, inhibit (antagonist), or decrease activity of the polypeptide or the molecule bound. Examples of such molecules include antibodies, oligonucleotides, proteins (e.g., receptors), or small molecules.

Preferably, the molecule is closely related to the natural ligand of the polypeptide, e.g., a fragment of the ligand, or a natural substrate, a ligand, a structural or functional mimetic. (See, Coligan et al., Current Protocols in Immunology 1(2):Chapter 5 (1991)). Similarly, the molecule can be closely related to the natural receptor to which the polypeptide binds, or at least, a fragment of the receptor capable of being bound by the polypeptide (e.g., active site). In either case, the molecule can be rationally designed using known techniques.

Preferably, the screening for these molecules involves producing appropriate cells which express the polypeptide. Preferred cells include cells from mammals, yeast, *Drosophila*, or *E. coli*. Cells expressing the polypeptide (or cell membrane containing the expressed polypeptide) are then preferably contacted with a test compound potentially containing the molecule to observe binding, stimulation, or inhibition of activity of either the polypeptide or the molecule.

The assay may simply test binding of a candidate compound to the polypeptide, wherein binding is detected by a label, or in an assay involving competition with a labeled competitor. Further, the assay may test whether the candidate compound results in a signal generated by binding to the polypeptide.

Alternatively, the assay can be carried out using cell-free preparations, polypeptide/molecule affixed to a solid support, chemical libraries, or natural product mixtures. The assay may also simply comprise the steps of mixing a candidate compound with a solution

containing a polypeptide, measuring polypeptide/molecule activity or binding, and comparing the polypeptide/molecule activity or binding to a standard.

Preferably, an ELISA assay can measure polypeptide level or activity in a sample (e.g., biological sample) using a monoclonal or polyclonal antibody. The antibody can measure
5 polypeptide level or activity by either binding, directly or indirectly, to the polypeptide or by competing with the polypeptide for a substrate.

Additionally, the receptor to which the polypeptide of the present invention binds can be identified by numerous methods known to those of skill in the art, for example, ligand panning and FACS sorting (Coligan, et al., *Current Protocols in Immun.*, 1(2), Chapter 5, (1991)). For
10 example, expression cloning is employed wherein polyadenylated RNA is prepared from a cell responsive to the polypeptides, for example, NIH3T3 cells which are known to contain multiple receptors for the FGF family proteins, and SC-3 cells, and a cDNA library created from this RNA is divided into pools and used to transfect COS cells or other cells that are not responsive to the polypeptides. Transfected cells which are grown on glass slides are exposed to the polypeptide of
15 the present invention, after they have been labeled. The polypeptides can be labeled by a variety of means including iodination or inclusion of a recognition site for a site-specific protein kinase.

Following fixation and incubation, the slides are subjected to auto-radiographic analysis. Positive pools are identified and sub-pools are prepared and re-transfected using an iterative sub-pooling and re-screening process, eventually yielding a single clones that encodes the putative
20 receptor.

As an alternative approach for receptor identification, the labeled polypeptides can be photoaffinity linked with cell membrane or extract preparations that express the receptor molecule. Cross-linked material is resolved by PAGE analysis and exposed to X-ray film. The labeled complex containing the receptors of the polypeptides can be excised, resolved into peptide
25 fragments, and subjected to protein microsequencing. The amino acid sequence obtained from microsequencing would be used to design a set of degenerate oligonucleotide probes to screen a cDNA library to identify the genes encoding the putative receptors.

Moreover, the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling") may be employed to modulate the
30 activities of the polypeptide of the present invention thereby effectively generating agonists and antagonists of the polypeptide of the present invention. *See generally*, U.S. Patent Nos. 5,605,793, 5,811,238, 5,830,721, 5,834,252, and 5,837,458, and Patten, P. A., et al., *Curr. Opinion Biotechnol.* 8:724-33 (1997); Harayama, S. *Trends Biotechnol.* 16(2):76-82 (1998); Hansson, L. O., et al., *J. Mol. Biol.* 287:265-76 (1999); and Lorenzo, M. M. and Blasco, R. *Biotechniques*
35 24(2):308-13 (1998); each of these patents and publications are hereby incorporated by reference. In one embodiment, alteration of polynucleotides and corresponding polypeptides may be achieved by DNA shuffling. DNA shuffling involves the assembly of two or more DNA segments

into a desired molecule by homologous, or site-specific, recombination. In another embodiment, polynucleotides and corresponding polypeptides may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of the polypeptide of the present invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules. In preferred embodiments, the heterologous molecules are family members. In further preferred embodiments, the heterologous molecule is a growth factor such as, for example, platelet-derived growth factor (PDGF), insulin-like growth factor (IGF-I), transforming growth factor (TGF)-alpha, epidermal growth factor (EGF), fibroblast growth factor (FGF), TGF-beta, bone morphogenetic protein (BMP)-2, BMP-4, BMP-5, BMP-6, BMP-7, activins A and B, decapentaplegic(dpp), 60A, OP-2, dorsalin, growth differentiation factors (GDFs), nodal, MIS, inhibin-alpha, TGF-beta1, TGF-beta2, TGF-beta3, TGF-beta5, and glial-derived neurotrophic factor (GDNF).

Other preferred fragments are biologically active fragments of the polypeptide of the present invention. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

Additionally, this invention provides a method of screening compounds to identify those which modulate the action of the polypeptide of the present invention. An example of such an assay comprises combining a mammalian fibroblast cell, a the polypeptide of the present invention, the compound to be screened and $^3\text{[H]}$ thymidine under cell culture conditions where the fibroblast cell would normally proliferate. A control assay may be performed in the absence of the compound to be screened and compared to the amount of fibroblast proliferation in the presence of the compound to determine if the compound stimulates proliferation by determining the uptake of $^3\text{[H]}$ thymidine in each case. The amount of fibroblast cell proliferation is measured by liquid scintillation chromatography which measures the incorporation of $^3\text{[H]}$ thymidine. Both agonist and antagonist compounds may be identified by this procedure.

In another method, a mammalian cell or membrane preparation expressing a receptor for a polypeptide of the present invention is incubated with a labeled polypeptide of the present invention in the presence of the compound. The ability of the compound to enhance or block this interaction could then be measured. Alternatively, the response of a known second messenger system following interaction of a compound to be screened and the receptor is measured and the ability of the compound to bind to the receptor and elicit a second messenger response is measured to determine if the compound is a potential agonist or antagonist. Such second messenger systems

include but are not limited to, cAMP guanylate cyclase, ion channels or phosphoinositide hydrolysis.

5 All of these above assays can be used as diagnostic or prognostic markers. The molecules discovered using these assays can be used to treat disease or to bring about a particular result in a patient (e.g., blood vessel growth) by activating or inhibiting the polypeptide/molecule. Moreover, the assays can discover agents which may inhibit or enhance the production of the polypeptides of the invention from suitably manipulated cells or tissues.

10 Therefore, the invention includes a method of identifying compounds which bind to a polypeptide of the invention comprising the steps of: (a) incubating a candidate binding compound with a polypeptide of the present invention; and (b) determining if binding has occurred. Moreover, the invention includes a method of identifying agonists/antagonists comprising the steps of: (a) incubating a candidate compound with a polypeptide of the present invention, (b) assaying a biological activity, and (b) determining if a biological activity of the polypeptide has been altered.

15

Targeted Delivery

In another embodiment, the invention provides a method of delivering compositions to targeted cells expressing a receptor for a polypeptide of the invention, or cells expressing a cell bound form of a polypeptide of the invention.

20 As discussed herein, polypeptides or antibodies of the invention may be associated with heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs via hydrophobic, hydrophilic, ionic and/or covalent interactions. In one embodiment, the invention provides a method for the specific delivery of compositions of the invention to cells by administering polypeptides of the invention (including antibodies) that are associated with heterologous polypeptides or nucleic acids. In one example, the invention provides a method for delivering a therapeutic protein into the targeted cell. In another example, the invention provides a method for delivering a single stranded nucleic acid (e.g., antisense or ribozymes) or double stranded nucleic acid (e.g., DNA that can integrate into the cell's genome or replicate episomally and that can be transcribed) into the targeted cell.

25 30 In another embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention (e.g., polypeptides of the invention or antibodies of the invention) in association with toxins or cytotoxic prodrugs.

35 By "toxin" is meant compounds that bind and activate endogenous cytotoxic effector systems, radioisotopes, holotoxins, modified toxins, catalytic subunits of toxins, or any molecules or enzymes not normally present in or on the surface of a cell that under

defined conditions cause the cell's death. Toxins that may be used according to the methods of the invention include, but are not limited to, radioisotopes known in the art, compounds such as, for example, antibodies (or complement fixing containing portions thereof) that bind an inherent or induced endogenous cytotoxic effector system, thymidine
5 kinase, endonuclease, RNase, alpha toxin, ricin, abrin, *Pseudomonas* exotoxin A, diphtheria toxin, saporin, momordin, gelonin, pokeweed antiviral protein, alpha-sarcin and cholera toxin. By "cytotoxic prodrug" is meant a non-toxic compound that is converted by an enzyme, normally present in the cell, into a cytotoxic compound. Cytotoxic
10 prodrugs that may be used according to the methods of the invention include, but are not limited to, glutamyl derivatives of benzoic acid mustard alkylating agent, phosphate derivatives of etoposide or mitomycin C, cytosine arabinoside, daunorubisin, and phenoxyacetamide derivatives of doxorubicin.

Drug Screening

15 Further contemplated is the use of the polypeptides of the present invention, or the polynucleotides encoding these polypeptides, to screen for molecules which modify the activities of the polypeptides of the present invention. Such a method would include contacting the polypeptide of the present invention with a selected compound(s) suspected of having antagonist or agonist activity, and assaying the activity of these polypeptides following binding.

20 This invention is particularly useful for screening therapeutic compounds by using the polypeptides of the present invention, or binding fragments thereof, in any of a variety of drug screening techniques. The polypeptide or fragment employed in such a test may be affixed to a solid support, expressed on a cell surface, free in solution, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with
25 recombinant nucleic acids expressing the polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. One may measure, for example, the formulation of complexes between the agent being tested and a polypeptide of the present invention.

Thus, the present invention provides methods of screening for drugs or any other agents
30 which affect activities mediated by the polypeptides of the present invention. These methods comprise contacting such an agent with a polypeptide of the present invention or a fragment thereof and assaying for the presence of a complex between the agent and the polypeptide or a fragment thereof, by methods well known in the art. In such a competitive binding assay, the agents to screen are typically labeled. Following incubation, free agent is separated from that
35 present in bound form, and the amount of free or uncomplexed label is a measure of the ability of a particular agent to bind to the polypeptides of the present invention.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to the polypeptides of the present invention, and is described in great detail in European Patent Application 84/03564, published on September 13, 1984, which is incorporated herein by reference herein. Briefly stated, large numbers of different small peptide
5 test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. The peptide test compounds are reacted with polypeptides of the present invention and washed. Bound polypeptides are then detected by methods well known in the art. Purified polypeptides are coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies may be used to capture the peptide and immobilize it on the solid
10 support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding polypeptides of the present invention specifically compete with a test compound for binding to the polypeptides or fragments thereof. In this manner, the antibodies are used to detect the presence of any peptide which shares one or more
15 antigenic epitopes with a polypeptide of the invention.

Antisense And Ribozyme (Antagonists)

In specific embodiments, antagonists according to the present invention are nucleic acids corresponding to the sequences contained in SEQ ID NO:X, or the complementary strand thereof,
20 and/or to cDNA sequences contained in cDNA ATCC Deposit No:Z identified for example, in Table 1A and/or 1B. In one embodiment, antisense sequence is generated internally, by the organism, in another embodiment, the antisense sequence is separately administered (see, for example, O'Connor, J., Neurochem. 56:560 (1991). Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988). Antisense technology can be
25 used to control gene expression through antisense DNA or RNA, or through triple-helix formation. Antisense techniques are discussed for example, in Okano, J., Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988). Triple helix formation is discussed in, for instance, Lee et al., Nucleic Acids Research 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1300
30 (1991). The methods are based on binding of a polynucleotide to a complementary DNA or RNA.

For example, the use of c-myc and c-myb antisense RNA constructs to inhibit the growth of the non-lymphocytic leukemia cell line HL-60 and other cell lines was previously described. (Wickstrom et al. (1988); Anfossi et al. (1989)). These experiments were performed *in vitro* by incubating cells with the oligoribonucleotide. A similar procedure for *in vivo* use is described in
35 WO 91/15580. Briefly, a pair of oligonucleotides for a given antisense RNA is produced as follows: A sequence complimentary to the first 15 bases of the open reading frame is flanked by an EcoRI site on the 5' end and a HindIII site on the 3' end. Next, the pair of oligonucleotides is

heated at 90°C for one minute and then annealed in 2X ligation buffer (20mM TRIS HCl pH 7.5, 10mM MgCl₂, 10mM dithiothreitol (DTT) and 0.2 mM ATP) and then ligated to the EcoRI/Hind III site of the retroviral vector PMV7 (WO 91/15580).

For example, the 5' coding portion of a polynucleotide that encodes the polypeptide of the present invention may be used to design an antisense RNA oligonucleotide of from about 10 to 40 base pairs in length. A DNA oligonucleotide is designed to be complementary to a region of the gene involved in transcription thereby preventing transcription and the production of the receptor. The antisense RNA oligonucleotide hybridizes to the mRNA *in vivo* and blocks translation of the mRNA molecule into receptor polypeptide.

In one embodiment, the antisense nucleic acid of the invention is produced intracellularly by transcription from an exogenous sequence. For example, a vector or a portion thereof, is transcribed, producing an antisense nucleic acid (RNA) of the invention. Such a vector would contain a sequence encoding the antisense nucleic acid. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired antisense RNA. Such vectors can be constructed by recombinant DNA technology methods standard in the art. Vectors can be plasmid, viral, or others known in the art, used for replication and expression in vertebrate cells. Expression of the sequence encoding the polypeptide of the present invention or fragments thereof, can be by any promoter known in the art to act in vertebrate, preferably human cells. Such promoters can be inducible or constitutive. Such promoters include, but are not limited to, the SV40 early promoter region (Bernoist and Chambon, Nature 29:304-310 (1981), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto et al., Cell 22:787-797 (1980), the herpes thymidine promoter (Wagner et al., Proc. Natl. Acad. Sci. U.S.A. 78:1441-1445 (1981), the regulatory sequences of the metallothionein gene (Brinster, et al., Nature 296:39-42 (1982)), etc.

The antisense nucleic acids of the invention comprise a sequence complementary to at least a portion of an RNA transcript of a gene of the present invention. However, absolute complementarity, although preferred, is not required. A sequence "complementary to at least a portion of an RNA," referred to herein, means a sequence having sufficient complementarity to be able to hybridize with the RNA, forming a stable duplex; in the case of double stranded antisense nucleic acids, a single strand of the duplex DNA may thus be tested, or triplex formation may be assayed. The ability to hybridize will depend on both the degree of complementarity and the length of the antisense nucleic acid. Generally, the larger the hybridizing nucleic acid, the more base mismatches with a RNA it may contain and still form a stable duplex (or triplex as the case may be). One skilled in the art can ascertain a tolerable degree of mismatch by use of standard procedures to determine the melting point of the hybridized complex.

Oligonucleotides that are complementary to the 5' end of the message, e.g., the 5' untranslated sequence up to and including the AUG initiation codon, should work most efficiently

at inhibiting translation. However, sequences complementary to the 3' untranslated sequences of mRNAs have been shown to be effective at inhibiting translation of mRNAs as well. See generally, Wagner, R., 1994, *Nature* 372:333-335. Thus, oligonucleotides complementary to either the 5'- or 3'- non- translated, non-coding regions of polynucleotide sequences described
 5 herein could be used in an antisense approach to inhibit translation of endogenous mRNA. Oligonucleotides complementary to the 5' untranslated region of the mRNA should include the complement of the AUG start codon. Antisense oligonucleotides complementary to mRNA coding regions are less efficient inhibitors of translation but could be used in accordance with the invention. Whether designed to hybridize to the 5'-, 3'- or coding region of mRNA of the present
 10 invention, antisense nucleic acids should be at least six nucleotides in length, and are preferably oligonucleotides ranging from 6 to about 50 nucleotides in length. In specific aspects the oligonucleotide is at least 10 nucleotides, at least 17 nucleotides, at least 25 nucleotides or at least 50 nucleotides.

The polynucleotides of the invention can be DNA or RNA or chimeric mixtures or
 15 derivatives or modified versions thereof, single-stranded or double-stranded. The oligonucleotide can be modified at the base moiety, sugar moiety, or phosphate backbone, for example, to improve stability of the molecule, hybridization, etc. The oligonucleotide may include other appended groups such as peptides (e.g., for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, e.g., Letsinger et al., 1989, *Proc. Natl. Acad. Sci. U.S.A.* 86:6553-6556; Lemaitre et al., 1987, *Proc. Natl. Acad. Sci.* 84:648-652; PCT Publication No.
 20 WO88/09810, published December 15, 1988) or the blood-brain barrier (see, e.g., PCT Publication No. WO89/10134, published April 25, 1988), hybridization-triggered cleavage agents. (See, e.g., Krol et al., 1988, *BioTechniques* 6:958-976) or intercalating agents. (See, e.g., Zon, 1988, *Pharm. Res.* 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, e.g., a
 25 peptide, hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

The antisense oligonucleotide may comprise at least one modified base moiety which is selected from the group including, but not limited to, 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil,
 30 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-
 35 isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-

carboxypurine, (acp3)w, and 2,6-diaminopurine.

The antisense oligonucleotide may also comprise at least one modified sugar moiety selected from the group including, but not limited to, arabinose, 2-fluoroarabinose, xylulose, and hexose.

5 In yet another embodiment, the antisense oligonucleotide comprises at least one modified phosphate backbone selected from the group including, but not limited to, a phosphorothioate, a phosphorodithioate, a phosphoramidothioate, a phosphoramidate, a phosphordiamidate, a methylphosphonate, an alkyl phosphotriester, and a formacetal or analog thereof.

10 In yet another embodiment, the antisense oligonucleotide is an a-anomeric oligonucleotide. An a-anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual b-units, the strands run parallel to each other (Gautier et al., 1987, Nucl. Acids Res. 15:6625-6641). The oligonucleotide is a 2'-O-methylribonucleotide (Inoue et al., 1987, Nucl. Acids Res. 15:6131-6148), or a chimeric RNA-DNA analogue (Inoue et al., 1987, FEBS Lett. 215:327-330).

15 Polynucleotides of the invention may be synthesized by standard methods known in the art, e.g. by use of an automated DNA synthesizer (such as are commercially available from Biosearch, Applied Biosystems, etc.). As examples, phosphorothioate oligonucleotides may be synthesized by the method of Stein et al. (1988, Nucl. Acids Res. 16:3209), methylphosphonate oligonucleotides can be prepared by use of controlled pore glass polymer supports (Sarin et al., 20 1988, Proc. Natl. Acad. Sci. U.S.A. 85:7448-7451), etc.

While antisense nucleotides complementary to the coding region sequence could be used, those complementary to the transcribed untranslated region are most preferred.

Potential antagonists according to the invention also include catalytic RNA, or a ribozyme (See, e.g., PCT International Publication WO 90/11364, published October 4, 1990; Sarver et al, 25 Science 247:1222-1225 (1990). While ribozymes that cleave mRNA at site specific recognition sequences can be used to destroy mRNAs, the use of hammerhead ribozymes is preferred. Hammerhead ribozymes cleave mRNAs at locations dictated by flanking regions that form complementary base pairs with the target mRNA. The sole requirement is that the target mRNA have the following sequence of two bases: 5'-UG-3'. The construction and production of 30 hammerhead ribozymes is well known in the art and is described more fully in Haseloff and Gerlach, Nature 334:585-591 (1988). There are numerous potential hammerhead ribozyme cleavage sites within the nucleotide sequence of SEQ ID NO:X. Preferably, the ribozyme is engineered so that the cleavage recognition site is located near the 5' end of the mRNA; i.e., to increase efficiency and minimize the intracellular accumulation of non-functional mRNA 35 transcripts.

As in the antisense approach, the ribozymes of the invention can be composed of modified oligonucleotides (e.g., for improved stability, targeting, etc.) and should be delivered to cells

which express *in vivo*. DNA constructs encoding the ribozyme may be introduced into the cell in the same manner as described above for the introduction of antisense encoding DNA. A preferred method of delivery involves using a DNA construct "encoding" the ribozyme under the control of a strong constitutive promoter, such as, for example, pol III or pol II promoter, so that transfected
5 cells will produce sufficient quantities of the ribozyme to destroy endogenous messages and inhibit translation. Since ribozymes unlike antisense molecules, are catalytic, a lower intracellular concentration is required for efficiency.

Antagonist/agonist compounds may be employed to inhibit the cell growth and proliferation effects of the polypeptides of the present invention on neoplastic cells and tissues, i.e.
10 stimulation of angiogenesis of tumors, and, therefore, retard or prevent abnormal cellular growth and proliferation, for example, in tumor formation or growth.

The antagonist/agonist may also be employed to prevent hyper-vascular diseases, and prevent the proliferation of epithelial lens cells after extracapsular cataract surgery. Prevention of the mitogenic activity of the polypeptides of the present invention may also be desirable in cases
15 such as restenosis after balloon angioplasty.

The antagonist/agonist may also be employed to prevent the growth of scar tissue during wound healing.

The antagonist/agonist may also be employed to treat the diseases described herein.

Thus, the invention provides a method of treating disorders or diseases, including but not
20 limited to the disorders or diseases listed throughout this application, associated with overexpression of a polynucleotide of the present invention by administering to a patient (a) an antisense molecule directed to the polynucleotide of the present invention, and/or (b) a ribozyme directed to the polynucleotide of the present invention.

25 **Binding Peptides and Other Molecules**

The invention also encompasses screening methods for identifying polypeptides and nonpolypeptides that bind polypeptides of the invention, and the binding molecules identified thereby. These binding molecules are useful, for example, as agonists and antagonists of the polypeptides of the invention. Such agonists and antagonists can be used, in accordance with the
30 invention, in the therapeutic embodiments described in detail, below.

This method comprises the steps of:

contacting polypeptides of the invention with a plurality of molecules; and
identifying a molecule that binds the polypeptides of the invention.

The step of contacting the polypeptides of the invention with the plurality of molecules
35 may be effected in a number of ways. For example, one may contemplate immobilizing the polypeptides on a solid support and bringing a solution of the plurality of molecules in contact with the immobilized polypeptides. Such a procedure would be akin to an affinity

chromatographic process, with the affinity matrix being comprised of the immobilized polypeptides of the invention. The molecules having a selective affinity for the polypeptides can then be purified by affinity selection. The nature of the solid support, process for attachment of the polypeptides to the solid support, solvent, and conditions of the affinity isolation or selection are
5 largely conventional and well known to those of ordinary skill in the art.

Alternatively, one may also separate a plurality of polypeptides into substantially separate fractions comprising a subset of or individual polypeptides. For instance, one can separate the plurality of polypeptides by gel electrophoresis, column chromatography, or like method known to those of ordinary skill for the separation of polypeptides. The individual polypeptides can also be
10 produced by a transformed host cell in such a way as to be expressed on or about its outer surface (e.g., a recombinant phage). Individual isolates can then be "probed" by the polypeptides of the invention, optionally in the presence of an inducer should one be required for expression, to determine if any selective affinity interaction takes place between the polypeptides and the individual clone. Prior to contacting the polypeptides with each fraction comprising individual
15 polypeptides, the polypeptides could first be transferred to a solid support for additional convenience. Such a solid support may simply be a piece of filter membrane, such as one made of nitrocellulose or nylon. In this manner, positive clones could be identified from a collection of transformed host cells of an expression library, which harbor a DNA construct encoding a polypeptide having a selective affinity for polypeptides of the invention. Furthermore, the amino
20 acid sequence of the polypeptide having a selective affinity for the polypeptides of the invention can be determined directly by conventional means or the coding sequence of the DNA encoding the polypeptide can frequently be determined more conveniently. The primary sequence can then be deduced from the corresponding DNA sequence. If the amino acid sequence is to be determined from the polypeptide itself, one may use microsequencing techniques. The sequencing technique
25 may include mass spectroscopy.

In certain situations, it may be desirable to wash away any unbound polypeptides from a mixture of the polypeptides of the invention and the plurality of polypeptides prior to attempting to determine or to detect the presence of a selective affinity interaction. Such a wash step may be particularly desirable when the polypeptides of the invention or the plurality of polypeptides are
30 bound to a solid support.

The plurality of molecules provided according to this method may be provided by way of diversity libraries, such as random or combinatorial peptide or nonpeptide libraries which can be screened for molecules that specifically bind polypeptides of the invention. Many libraries are known in the art that can be used, e.g., chemically synthesized libraries, recombinant (e.g., phage
35 display libraries), and in vitro translation-based libraries. Examples of chemically synthesized libraries are described in Fodor et al., 1991, Science 251:767-773; Houghten et al., 1991, Nature 354:84-86; Lam et al., 1991, Nature 354:82-84; Medynski, 1994, Bio/Technology 12:709-

710; Gallop et al., 1994, *J. Medicinal Chemistry* 37(9):1233-1251; Ohlmeyer et al., 1993, *Proc. Natl. Acad. Sci. USA* 90:10922-10926; Erb et al., 1994, *Proc. Natl. Acad. Sci. USA* 91:11422-11426; Houghten et al., 1992, *Biotechniques* 13:412; Jayawickreme et al., 1994, *Proc. Natl. Acad. Sci. USA* 91:1614-1618; Salmon et al., 1993, *Proc. Natl. Acad. Sci. USA* 90:11708-11712; PCT
5 Publication No. WO 93/20242; and Brenner and Lerner, 1992, *Proc. Natl. Acad. Sci. USA* 89:5381-5383.

Examples of phage display libraries are described in Scott and Smith, 1990, *Science* 249:386-390; Devlin et al., 1990, *Science*, 249:404-406; Christian, R. B., et al., 1992, *J. Mol. Biol.* 227:711-718; Lenstra, 1992, *J. Immunol. Meth.* 152:149-157; Kay et al., 1993, *Gene* 128:59-65;
10 and PCT Publication No. WO 94/18318 dated Aug. 18, 1994.

In vitro translation-based libraries include but are not limited to those described in PCT Publication No. WO 91/05058 dated Apr. 18, 1991; and Mattheakis et al., 1994, *Proc. Natl. Acad. Sci. USA* 91:9022-9026.

By way of examples of nonpeptide libraries, a benzodiazepine library (see e.g., Bunin et al., 1994, *Proc. Natl. Acad. Sci. USA* 91:4708-4712) can be adapted for use. Peptoid libraries (Simon et al., 1992, *Proc. Natl. Acad. Sci. USA* 89:9367-9371) can also be used. Another example of a library that can be used, in which the amide functionalities in peptides have been permethylated to generate a chemically transformed combinatorial library, is described by Ostresh et al. (1994, *Proc. Natl. Acad. Sci. USA* 91:11138-11142).
15

The variety of non-peptide libraries that are useful in the present invention is great. For example, Ecker and Crooke, 1995, *Bio/Technology* 13:351-360 list benzodiazepines, hydantoins, piperazinediones, biphenyls, sugar analogs, beta-mercaptoketones, arylacetic acids, acylpiperidines, benzopyrans, cubanes, xanthines, aminimides, and oxazolones as among the chemical species that form the basis of various libraries.
20

Non-peptide libraries can be classified broadly into two types: decorated monomers and oligomers. Decorated monomer libraries employ a relatively simple scaffold structure upon which a variety functional groups is added. Often the scaffold will be a molecule with a known useful pharmacological activity. For example, the scaffold might be the benzodiazepine structure.
25

Non-peptide oligomer libraries utilize a large number of monomers that are assembled together in ways that create new shapes that depend on the order of the monomers. Among the monomer units that have been used are carbamates, pyrrolinones, and morpholinos. Peptoids, peptide-like oligomers in which the side chain is attached to the alpha amino group rather than the alpha carbon, form the basis of another version of non-peptide oligomer libraries. The first non-peptide oligomer libraries utilized a single type of monomer and thus contained a repeating backbone. Recent libraries have utilized more than one monomer, giving the libraries added flexibility.
30
35

Screening the libraries can be accomplished by any of a variety of commonly known

methods. See, e.g., the following references, which disclose screening of peptide libraries: Parmley and Smith, 1989, *Adv. Exp. Med. Biol.* 251:215-218; Scott and Smith, 1990, *Science* 249:386-390; Fowlkes et al., 1992, *BioTechniques* 13:422-427; Oldenburg et al., 1992, *Proc. Natl. Acad. Sci. USA* 89:5393-5397; Yu et al., 1994, *Cell* 76:933-945; Staudt et al., 1988, *Science* 241:577-580; Bock et al., 1992, *Nature* 355:564-566; Tuerk et al., 1992, *Proc. Natl. Acad. Sci. USA* 89:6988-6992; Ellington et al., 1992, *Nature* 355:850-852; U.S. Pat. No. 5,096,815, U.S. Pat. No. 5,223,409, and U.S. Pat. No. 5,198,346, all to Ladner et al.; Rebar and Pabo, 1993, *Science* 263:671-673; and CT Publication No. WO 94/18318.

In a specific embodiment, screening to identify a molecule that binds polypeptides of the invention can be carried out by contacting the library members with polypeptides of the invention immobilized on a solid phase and harvesting those library members that bind to the polypeptides of the invention. Examples of such screening methods, termed "panning" techniques are described by way of example in Parmley and Smith, 1988, *Gene* 73:305-318; Fowlkes et al., 1992, *BioTechniques* 13:422-427; PCT Publication No. WO 94/18318; and in references cited herein.

In another embodiment, the two-hybrid system for selecting interacting proteins in yeast (Fields and Song, 1989, *Nature* 340:245-246; Chien et al., 1991, *Proc. Natl. Acad. Sci. USA* 88:9578-9582) can be used to identify molecules that specifically bind to polypeptides of the invention.

Where the binding molecule is a polypeptide, the polypeptide can be conveniently selected from any peptide library, including random peptide libraries, combinatorial peptide libraries, or biased peptide libraries. The term "biased" is used herein to mean that the method of generating the library is manipulated so as to restrict one or more parameters that govern the diversity of the resulting collection of molecules, in this case peptides.

Thus, a truly random peptide library would generate a collection of peptides in which the probability of finding a particular amino acid at a given position of the peptide is the same for all 20 amino acids. A bias can be introduced into the library, however, by specifying, for example, that a lysine occur every fifth amino acid or that positions 4, 8, and 9 of a decapeptide library be fixed to include only arginine. Clearly, many types of biases can be contemplated, and the present invention is not restricted to any particular bias. Furthermore, the present invention contemplates specific types of peptide libraries, such as phage displayed peptide libraries and those that utilize a DNA construct comprising a lambda phage vector with a DNA insert.

As mentioned above, in the case of a binding molecule that is a polypeptide, the polypeptide may have about 6 to less than about 60 amino acid residues, preferably about 6 to about 10 amino acid residues, and most preferably, about 6 to about 22 amino acids. In another embodiment, a binding polypeptide has in the range of 15-100 amino acids, or 20-50 amino acids.

The selected binding polypeptide can be obtained by chemical synthesis or recombinant expression.

Other Activities

A polypeptide, polynucleotide, agonist, or antagonist of the present invention, as a result of the ability to stimulate vascular endothelial cell growth, may be employed in treatment for
5 stimulating re-vascularization of ischemic tissues due to various disease conditions such as thrombosis, arteriosclerosis, and other cardiovascular conditions. The polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed to stimulate angiogenesis and limb regeneration, as discussed above.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be
10 employed for treating wounds due to injuries, burns, post-operative tissue repair, and ulcers since they are mitogenic to various cells of different origins, such as fibroblast cells and skeletal muscle cells, and therefore, facilitate the repair or replacement of damaged or diseased tissue.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed stimulate neuronal growth and to treat and prevent neuronal damage which occurs in
15 certain neuronal disorders or neuro-degenerative conditions such as Alzheimer's disease, Parkinson's disease, and AIDS-related complex. A polypeptide, polynucleotide, agonist, or antagonist of the present invention may have the ability to stimulate chondrocyte growth, therefore, they may be employed to enhance bone and periodontal regeneration and aid in tissue transplants or bone grafts.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may be also
20 be employed to prevent skin aging due to sunburn by stimulating keratinocyte growth.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed for preventing hair loss, since FGF family members activate hair-forming cells and promotes melanocyte growth. Along the same lines, a polypeptide, polynucleotide, agonist, or
25 antagonist of the present invention may be employed to stimulate growth and differentiation of hematopoietic cells and bone marrow cells when used in combination with other cytokines.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed to maintain organs before transplantation or for supporting cell culture of primary tissues. A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be
30 employed for inducing tissue of mesodermal origin to differentiate in early embryos.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also increase or decrease the differentiation or proliferation of embryonic stem cells, besides, as discussed above, hematopoietic lineage.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be
35 used to modulate mammalian characteristics, such as body height, weight, hair color, eye color, skin, percentage of adipose tissue, pigmentation, size, and shape (e.g., cosmetic surgery). Similarly, a polypeptide, polynucleotide, agonist, or antagonist of the present invention may be

used to modulate mammalian metabolism affecting catabolism, anabolism, processing, utilization, and storage of energy.

5 A polypeptide, polynucleotide, agonist, or antagonist of the present invention may be used to change a mammal's mental state or physical state by influencing biorhythms, cardiac rhythms, depression (including depressive disorders), tendency for violence, tolerance for pain, reproductive capabilities (preferably by Activin or Inhibin-like activity), hormonal or endocrine levels, appetite, libido, memory, stress, or other cognitive qualities.

10 A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be used as a food additive or preservative, such as to increase or decrease storage capabilities, fat content, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional components.

The above-recited applications have uses in a wide variety of hosts. Such hosts include, but are not limited to, human, murine, rabbit, goat, guinea pig, camel, horse, mouse, rat, hamster, pig, micro-pig, chicken, goat, cow, sheep, dog, cat, non-human primate, and human. In specific embodiments, the host is a mouse, rabbit, goat, guinea pig, chicken, rat, hamster, pig, sheep, dog
15 or cat. In preferred embodiments, the host is a mammal. In most preferred embodiments, the host is a human.

Other Preferred Embodiments

20 Other preferred embodiments of the claimed invention include an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 50 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, the nucleotide sequence as defined in Table 1B or columns 8 and 9 of Table 2 or the complementary strand thereto, and/or cDNA contained in ATCC Deposit No:Z.

25 Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of the portion of SEQ ID NO:X as defined in column 5, "ORF (From-To)", in Table 1B.1.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of the portion of SEQ ID NO:X as defined in columns 8 and 9, "NT From" and "NT To" respectively, in Table 2.

30 Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 150 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, the nucleotide sequence as defined in Table 1B or columns 8 and 9 of Table 2 or the complementary strand thereto, and/or cDNA contained in ATCC Deposit No:Z.

35 Further preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 500 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, the nucleotide

sequence as defined in Table 1B or columns 8 and 9 of Table 2 or the complementary strand thereto, and/or cDNA contained in ATCC Deposit No:Z.

5 A further preferred embodiment is a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the nucleotide sequence of the portion of SEQ ID NO:X defined in column 5, "ORF (From-To)", in Table 1B.1.

A further preferred embodiment is a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the nucleotide sequence of the portion of SEQ ID NO:X defined in columns 8 and 9, "NT From" and "NT To", respectively, in Table 2.

10 A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, the nucleotide sequence as defined in column 5 of Table 1B.1 or columns 8 and 9 of Table 2 or the complementary strand thereto, and/or cDNA contained in ATCC Deposit No:Z.

15 Also preferred is an isolated nucleic acid molecule which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, the nucleotide sequence as defined in column 5 of Table 1B.1 or columns 8 and 9 of Table 2 or the complementary strand thereto, and/or cDNA contained in ATCC Deposit No:Z, wherein said nucleic acid molecule which hybridizes does not hybridize under stringent hybridization conditions to a nucleic acid molecule having a nucleotide
20 sequence consisting of only A residues or of only T residues.

Also preferred is a composition of matter comprising a DNA molecule which comprises the cDNA contained in ATCC Deposit No:Z.

25 Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides of the cDNA sequence contained in ATCC Deposit No:Z.

Also preferred is an isolated nucleic acid molecule, wherein said sequence of at least 50 contiguous nucleotides is included in the nucleotide sequence of an open reading frame sequence encoded by cDNA contained in ATCC Deposit No:Z.

30 Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 150 contiguous nucleotides in the nucleotide sequence encoded by cDNA contained in ATCC Deposit No:Z.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 500 contiguous nucleotides in the nucleotide sequence encoded by cDNA contained in ATCC Deposit No:Z.

35 A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence encoded by cDNA contained in ATCC Deposit No:Z.

A further preferred embodiment is a method for detecting in a biological sample a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; the nucleotide sequence as defined in column 5 of Table 1B.1 or columns 8 and 9 of Table 2 or the complementary strand thereto; and a nucleotide sequence encoded by cDNA contained in ATCC Deposit No:Z; which method comprises a step of comparing a nucleotide sequence of at least one nucleic acid molecule in said sample with a sequence selected from said group and determining whether the sequence of said nucleic acid molecule in said sample is at least 95% identical to said selected sequence.

Also preferred is the above method wherein said step of comparing sequences comprises determining the extent of nucleic acid hybridization between nucleic acid molecules in said sample and a nucleic acid molecule comprising said sequence selected from said group. Similarly, also preferred is the above method wherein said step of comparing sequences is performed by comparing the nucleotide sequence determined from a nucleic acid molecule in said sample with said sequence selected from said group. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

A further preferred embodiment is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting nucleic acid molecules in said sample, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; the nucleotide sequence as defined in column 5 of Table 1B.1 or columns 8 and 9 of Table 2 or the complementary strand thereto; and a nucleotide sequence of the cDNA contained in ATCC Deposit No:Z.

The method for identifying the species, tissue or cell type of a biological sample can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; the nucleotide sequence as defined in column 5 of Table 1B.1 or columns 8 and 9 of Table 2 or the complementary strand thereto; or the cDNA contained in ATCC Deposit No:Z which encodes a protein, wherein the method comprises a step of detecting in a biological sample obtained from said subject nucleic acid molecules, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; the nucleotide sequence as defined in column 5 of

Table 1B.1 or columns 8 and 9 of Table 2 or the complementary strand thereto; and a nucleotide sequence of cDNA contained in ATCC Deposit No:Z.

5 The method for diagnosing a pathological condition can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of:
10 a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; the nucleotide sequence as defined in column 5 of Table 1B.1 or columns 8 and 9 of Table 2 or the complementary strand thereto; and a nucleotide sequence encoded by cDNA contained in ATCC Deposit No:Z. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a DNA microarray or "chip" of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 40, 50, 100, 150, 200, 250, 300, 500, 1000, 2000, 3000, or 4000 nucleotide sequences, wherein at least one sequence in said DNA microarray or "chip" is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein
20 X is any integer as defined in Table 1A and/or 1B; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA "Clone ID" in Table 1A and/or 1B.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2; and/or
25 a polypeptide encoded by cDNA contained in ATCC Deposit No:Z.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2; and/or
30 a polypeptide encoded by cDNA contained in ATCC Deposit No:Z.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2; and/or a polypeptide encoded by cDNA contained in ATCC Deposit No:Z.
35

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the complete amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2; and/or a polypeptide encoded by cDNA
5 contained in ATCC Deposit No:Z.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the complete amino acid sequence of a polypeptide encoded by contained in ATCC Deposit No:Z

Also preferred is a polypeptide wherein said sequence of contiguous amino acids is
10 included in the amino acid sequence of a portion of said polypeptide encoded by cDNA contained in ATCC Deposit No:Z; a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2; and/or the polypeptide sequence of SEQ ID NO:Y.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95%
15 identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of a polypeptide encoded by cDNA contained in ATCC Deposit No:Z.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95%
20 identical to the amino acid sequence of a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z.

Further preferred is an isolated antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10
25 contiguous amino acids in a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2; and a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z.

Further preferred is a method for detecting in a biological sample a polypeptide
30 comprising an amino acid sequence which is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2; and a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z; which
35 method comprises a step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group and determining whether the

sequence of said polypeptide molecule in said sample is at least 90% identical to said sequence of at least 10 contiguous amino acids.

Also preferred is the above method wherein said step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group comprises determining the extent of specific binding of polypeptides in said sample to an antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2; and a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z.

Also preferred is the above method wherein said step of comparing sequences is performed by comparing the amino acid sequence determined from a polypeptide molecule in said sample with said sequence selected from said group.

Also preferred is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting polypeptide molecules in said sample, if any, comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2; and a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample, which method comprises a step of detecting polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the above group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a nucleic acid sequence identified in Table 1A, 1B or Table 2 encoding a polypeptide, which method comprises a step of detecting in a biological sample obtained from said subject polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2; and a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z.

In any of these methods, the step of detecting said polypeptide molecules includes using an antibody.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleotide sequence encoding a polypeptide wherein said polypeptide comprises an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2; and a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z.

Also preferred is an isolated nucleic acid molecule, wherein said nucleotide sequence encoding a polypeptide has been optimized for expression of said polypeptide in a prokaryotic host.

Also preferred is a polypeptide molecule, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2; and a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z.

Further preferred is a method of making a recombinant vector comprising inserting any of the above isolated nucleic acid molecule into a vector. Also preferred is the recombinant vector produced by this method. Also preferred is a method of making a recombinant host cell comprising introducing the vector into a host cell, as well as the recombinant host cell produced by this method.

Also preferred is a method of making an isolated polypeptide comprising culturing this recombinant host cell under conditions such that said polypeptide is expressed and recovering said polypeptide. Also preferred is this method of making an isolated polypeptide, wherein said recombinant host cell is a eukaryotic cell and said polypeptide is a human protein comprising an amino acid sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2; and a polypeptide encoded by the cDNA contained in ATCC Deposit No:Z. The isolated polypeptide produced by this method is also preferred.

Also preferred is a method of treatment of an individual in need of an increased level of a protein activity, which method comprises administering to such an individual a Therapeutic comprising an amount of an isolated polypeptide, polynucleotide, immunogenic fragment or analogue thereof, binding agent, antibody, or antigen binding fragment of the claimed invention effective to increase the level of said protein activity in said individual.

Also preferred is a method of treatment of an individual in need of a decreased level of a protein activity, which method comprised administering to such an individual a Therapeutic comprising an amount of an isolated polypeptide, polynucleotide, immunogenic fragment or analogue thereof, binding agent, antibody, or antigen binding fragment of the claimed invention effective to decrease the level of said protein activity in said individual.

Also preferred is a method of treatment of an individual in need of a specific delivery of toxic compositions to diseased cells (e.g., tumors, leukemias or lymphomas), which method comprises administering to such an individual a Therapeutic comprising an amount of an isolated polypeptide of the invention, including, but not limited to a binding agent, or antibody of the claimed invention that are associated with toxin or cytotoxic prodrugs.

Having generally described the invention, the same will be more readily understood by reference to the following examples, which are provided by way of illustration and are not intended as limiting.

15 Description of Table 6

Table 6 summarizes some of the ATCC Deposits, Deposit dates, and ATCC designation numbers of deposits made with the ATCC in connection with the present application. These deposits were made in addition to those described in the Table 1A.

20 Table 6

ATCC Deposits	Deposit Date	ATCC Designation Number
LP01, LP02, LP03, LP04, LP05, LP06, LP07, LP08, LP09, LP10, LP11,	May-20-97	209059, 209060, 209061, 209062, 209063, 209064, 209065, 209066, 209067, 209068, 209069
LP12	Jan-12-98	209579
LP13	Jan-12-98	209578
LP14	Jul-16-98	203067
LP15	Jul-16-98	203068
LP16	Feb-1-99	203609
LP17	Feb-1-99	203610
LP20	Nov-17-98	203485
LP21	Jun-18-99	PTA-252
LP22	Jun-18-99	PTA-253
LP23	Dec-22-99	PTA-1081

*Examples**Example 1: Isolation of a Selected cDNA Clone From the Deposited Sample*

5 Each ATCC Deposit No:Z is contained in a plasmid vector. Table 7 identifies the vectors used to construct the cDNA library from which each clone was isolated. In many cases, the vector used to construct the library is a phage vector from which a plasmid has been excised. The following correlates the related plasmid for each phage vector used in constructing the cDNA library. For example, where a particular clone is identified in Table 7 as being isolated in the
 10 vector "Lambda Zap," the corresponding deposited clone is in "pBluescript."

	<u>Vector Used to Construct Library</u>	<u>Corresponding Deposited Plasmid</u>
	Lambda Zap	pBluescript (pBS)
	Uni-Zap XR	pBluescript (pBS)
	Zap Express	pBK
15	lafmid BA	plafmid BA
	pSport1	pSport1
	pCMVSPORT 2.0	pCMVSPORT 2.0
	pCMVSPORT 3.0	pCMVSPORT 3.0
	pCR [®] 2.1	pCR [®] 2.1
20	Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., Nucleic Acids Res. 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., Nucleic Acids Res. 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., Strategies 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 25 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Both can be transformed into E. coli strain XL-1 Blue, also available from Stratagene. pBS comes in 4 forms SK+, SK-, KS+ and KS-. The S and K refers to the orientation of the polylinker to the T7 and T3 primer sequences which flank the polylinker region ("S" is for SacI and "K" is for KpnI which are the first sites on each respective 30 end of the linker). "+" or "-" refer to the orientation of the f1 origin of replication ("ori"), such that in one orientation, single stranded rescue initiated from the f1 ori generates sense strand DNA and in the other, antisense.	

Vectors pSport1, pCMVSPORT 2.0 and pCMVSPORT 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an
 35 ampicillin resistance gene and may be transformed into E. coli strain DH10B, also available from Life Technologies. (See, for instance, Gruber, C. E., et al., Focus 15:59 (1993)). Vector lafmid BA (Bento Soares, Columbia University, NY) contains an ampicillin resistance gene and can be

transformed into *E. coli* strain XL-1 Blue. Vector pCR[®]2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, available from Life Technologies. (See, for instance, Clark, J. M., *Nuc. Acids Res.* 16:9677-9686 (1988) and Mead, D. et al., *Bio/Technology* 9: 5 (1991)). Preferably, a polynucleotide of the present invention does not comprise the phage vector sequences identified for the particular clone in Table 7, as well as the corresponding plasmid vector sequences designated above.

The deposited material in the sample assigned the ATCC Deposit Number cited by reference to Table 1A, Table 2, Table 6 and Table 7 for any given cDNA clone also may contain 10 one or more additional plasmids, each comprising a cDNA clone different from that given clone. Thus, deposits sharing the same ATCC Deposit Number contain at least a plasmid for each ATCC Deposit No:Z.

TABLE 7

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HUKA HUKB HUKC HUKD HUKF HUKG	Human Uterine Cancer	Lambda ZAP II	LP01
HCNA HCNB	Human Colon	Lambda Zap II	LP01
HFFA	Human Fetal Brain, random primed	Lambda Zap II	LP01
HTWA	Resting T-Cell	Lambda ZAP II	LP01
HBQA	Early Stage Human Brain, random primed	Lambda ZAP II	LP01
HLMB HLMF HLMG HLMH HLMJ HLMK HLMN	breast lymph node CDNA library	Lambda ZAP II	LP01
HCQA HCQB	human colon cancer	Lambda ZAP II	LP01
HMEA HMEC HMEF HMEG HMEI HMEJ HMEK HMEK	Human Microvascular Endothelial Cells, fract. A	Lambda ZAP II	LP01
HUSA HUSC	Human Umbilical Vein Endothelial Cells, fract. A	Lambda ZAP II	LP01
HLQA HLQB	Hepatocellular Tumor	Lambda ZAP II	LP01
HHGA HHGB HHGC HHGD	Hemangiopericytoma	Lambda ZAP II	LP01
HSDM	Human Striatum Depression, re-rescue	Lambda ZAP II	LP01
HUSH	H Umbilical Vein Endothelial Cells, frac A, re-excision	Lambda ZAP II	LP01
HSGS	Salivary gland, subtracted	Lambda ZAP II	LP01
HFXA HFXB HFXC HFXD HFXE HFXF HFXG HFXH	Brain frontal cortex	Lambda ZAP II	LP01
HPQA HPQB HPQC	PERM TF274	Lambda ZAP II	LP01
HFXJ HFXK	Brain Frontal Cortex, re-excision	Lambda ZAP II	LP01
HCWA HCWB HCWC HCWD HCWE HCWF HCWG HCWH HCWI HCWJ HCWK	CD34 positive cells (Cord Blood)	ZAP Express	LP02
HCUA HCUB HCUC	CD34 depleted Buffy Coat	ZAP Express	LP02

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
	(Cord Blood)		
HRSM	A-14 cell line	ZAP Express	LP02
HRSA	A1-CELL LINE	ZAP Express	LP02
HCUD HCUE HCUF HCUG HCUH HCUI	CD34 depleted Buffy Coat (Cord Blood), re-excision	ZAP Express	LP02
HBXE HBXF HBXG	H. Whole Brain #2, re-excision	ZAP Express	LP02
HRLM	L8 cell line	ZAP Express	LP02
HBXA HBXB HBXC HBXD	Human Whole Brain #2 - Oligo dT > 1.5Kb	ZAP Express	LP02
HUDA HUDB HUDC	Testes	ZAP Express	LP02
HHTM HHTN HHTO	H. hypothalamus, frac A; re- excision	ZAP Express	LP02
HHTL	H. hypothalamus, frac A	ZAP Express	LP02
HASA HASD	Human Adult Spleen	Uni-ZAP XR	LP03
HFKC HFKD HFKE HFKE HFKG	Human Fetal Kidney	Uni-ZAP XR	LP03
HE8A HE8B HE8C HE8D HE8E HE8F HE8M HE8N	Human 8 Week Whole Embryo	Uni-ZAP XR	LP03
HGBA HGBD HGBE HGBF HGBG HGBH HGBI	Human Gall Bladder	Uni-ZAP XR	LP03
HLHA HLHB HLHC HLHD HLHE HLHF HLHG HLHH HLHQ	Human Fetal Lung III	Uni-ZAP XR	LP03
HPMA HPMB HPMC HPMD HPME HPMF HPMG HPMH	Human Placenta	Uni-ZAP XR	LP03
HPRA HPRB HPRC HPRD	Human Prostate	Uni-ZAP XR	LP03
HSIA HSIC HSID HSIE	Human Adult Small Intestine	Uni-ZAP XR	LP03
HTEA HTEB HTEC HTED HTEE HTEF HTEG HTEH HTEI HTEJ HTEK	Human Testes	Uni-ZAP XR	LP03
HTPA HTPB HTPC HTPD HTPE	Human Pancreas Tumor	Uni-ZAP XR	LP03
HTTA HTTB HTTC HTTD HTTE HTTF	Human Testes Tumor	Uni-ZAP XR	LP03
HAPA HAPB HAPC HAPM	Human Adult Pulmonary	Uni-ZAP XR	LP03
HETA HETB HETC HETD HETE HETF HETG HETH HETI	Human Endometrial Tumor	Uni-ZAP XR	LP03
HHFB HHFC HHFD HHFE HHFF HHFG HHFH HHFI	Human Fetal Heart	Uni-ZAP XR	LP03
HHPB HHPD HHPD HHPD HHPF HHPG HHPH	Human Hippocampus	Uni-ZAP XR	LP03
HCE1 HCE2 HCE3 HCE4 HCE5 HCEB HCEC HCED HCEE HCEF HCEG	Human Cerebellum	Uni-ZAP XR	LP03
HUVB HUVB HUVB HUVB	Human Umbilical Vein, Endo. remake	Uni-ZAP XR	LP03
HSTA HSTB HSTC HSTD	Human Skin Tumor	Uni-ZAP XR	LP03
HTAA HTAB HTAC HTAD HTAE	Human Activated T-Cells	Uni-ZAP XR	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HFEA HFEB HFEC	Human Fetal Epithelium (Skin)	Uni-ZAP XR	LP03
HJPA HJPB HJPC HJPD	HUMAN JURKAT MEMBRANE BOUND POLYSOMES	Uni-ZAP XR	LP03
HESA	Human epithelioid sarcoma	Uni-Zap XR	LP03
HLTA HLTB HLTC HLTD HLTE HLTF	Human T-Cell Lymphoma	Uni-ZAP XR	LP03
HFTA HFTB HFTC HFTD	Human Fetal Dura Mater	Uni-ZAP XR	LP03
HRDA HRDB HRDC HRDD HRDE HRDF	Human Rhabdomyosarcoma	Uni-ZAP XR	LP03
HCAA HCAB HCAC	Cem cells cyclohexamide treated	Uni-ZAP XR	LP03
HRGA HRGB HRGC HRGD	Raji Cells, cyclohexamide treated	Uni-ZAP XR	LP03
HSUA HSUB HSUC HSUM	Supt Cells, cyclohexamide treated	Uni-ZAP XR	LP03
HT4A HT4C HT4D	Activated T-Cells, 12 hrs.	Uni-ZAP XR	LP03
HE9A HE9B HE9C HE9D HE9E HE9F HE9G HE9H HE9M HE9N	Nine Week Old Early Stage Human	Uni-ZAP XR	LP03
HATA HATB HATC HATD HATE	Human Adrenal Gland Tumor	Uni-ZAP XR	LP03
HT5A	Activated T-Cells, 24 hrs.	Uni-ZAP XR	LP03
HFGA HFGM	Human Fetal Brain	Uni-ZAP XR	LP03
HNEA HNEB HNEC HNED HNEE	Human Neutrophil	Uni-ZAP XR	LP03
HBGB HBGD	Human Primary Breast Cancer	Uni-ZAP XR	LP03
HBNA HBNB	Human Normal Breast	Uni-ZAP XR	LP03
HCAS	Cem Cells, cyclohexamide treated, subtra	Uni-ZAP XR	LP03
HHPS	Human Hippocampus, subtracted	pBS	LP03
HKCS HKCU	Human Colon Cancer, subtracted	pBS	LP03
HRGS	Raji cells, cyclohexamide treated, subtracted	pBS	LP03
HSUT	Supt cells, cyclohexamide treated, differentially expressed	pBS	LP03
HT4S	Activated T-Cells, 12 hrs, subtracted	Uni-ZAP XR	LP03
HCDA HCDB HCDC HCDD HCDE	Human Chondrosarcoma	Uni-ZAP XR	LP03
HOAA HOAB HOAC	Human Osteosarcoma	Uni-ZAP XR	LP03
HTLA HTLB HTLC HTLD HTLE HTLF	Human adult testis, large inserts	Uni-ZAP XR	LP03
HLMA HLMC HLMD	Breast Lymph node cDNA library	Uni-ZAP XR	LP03
H6EA H6EB H6EC	HL-60, PMA 4H	Uni-ZAP XR	LP03
HTXA HTXB HTXC HTXD HTXE HTXF HTXG HTXH	Activated T-Cell (12hs)/Thiouridine labelledEco	Uni-ZAP XR	LP03
HNFA HNFB HNFC HNFD	Human Neutrophil, Activated	Uni-ZAP XR	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HNFE HNFF HNFG HNFH HNFJ			
HTOB HTOC	HUMAN TONSILS, FRACTION 2	Uni-ZAP XR	LP03
HMGB	Human OB MG63 control fraction I	Uni-ZAP XR	LP03
HOPB	Human OB HOS control fraction I	Uni-ZAP XR	LP03
HORB	Human OB HOS treated (10 nM E2) fraction I	Uni-ZAP XR	LP03
HSVA HSVB HSVC	Human Chronic Synovitis	Uni-ZAP XR	LP03
HROA	HUMAN STOMACH	Uni-ZAP XR	LP03
HBJA HBJB HBJC HBJD HBJE HBJF HBJG HBJH HBJI HBJJ HBJK	HUMAN B CELL LYMPHOMA	Uni-ZAP XR	LP03
HCRA HCRB HCRC	human corpus colosum	Uni-ZAP XR	LP03
HODA HODB HODC HODD	human ovarian cancer	Uni-ZAP XR	LP03
HDSA	Dermatofibrosarcoma Protuberance	Uni-ZAP XR	LP03
HMWA HMWB HMWC HMWD HMWE HMWF HMWG HMWH HMWI HMWJ	Bone Marrow Cell Line (RS4;11)	Uni-ZAP XR	LP03
HSOA	stomach cancer (human)	Uni-ZAP XR	LP03
HERA	SKIN	Uni-ZAP XR	LP03
HMDA	Brain-medulloblastoma	Uni-ZAP XR	LP03
HGLA HGLB HGLD	Glioblastoma	Uni-ZAP XR	LP03
HEAA	H. Atrophic Endometrium	Uni-ZAP XR	LP03
HBCA HBCB	H. Lymph node breast Cancer	Uni-ZAP XR	LP03
HPWT	Human Prostate BPH, re-excision	Uni-ZAP XR	LP03
HFVG HFVH HFVI	Fetal Liver, subtraction II	pBS	LP03
HNFI	Human Neutrophils, Activated, re-excision	pBS	LP03
HBMB HBMC HBMD	Human Bone Marrow, re-excision	pBS	LP03
HKML HKMM HKMN	H. Kidney Medulla, re-excision	pBS	LP03
HKIX HKIY	H. Kidney Cortex, subtracted	pBS	LP03
HADT	H. Amygdala Depression, subtracted	pBS	LP03
H6AS	HL-60, untreated, subtracted	Uni-ZAP XR	LP03
H6ES	HL-60, PMA 4H, subtracted	Uni-ZAP XR	LP03
H6BS	HL-60, RA 4h, Subtracted	Uni-ZAP XR	LP03
H6CS	HL-60, PMA 1d, subtracted	Uni-ZAP XR	LP03
HTXJ HTXK	Activated T-cell(12h)/Thiouridine-re-excision	Uni-ZAP XR	LP03
HMSA HMSB HMSC HMSD HMSE HMSF HMSG HMSH HMSI HMSJ HMSK	Monocyte activated	Uni-ZAP XR	LP03
HAGA HAGB HAGC HAGD	Human Amygdala	Uni-ZAP XR	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HAGE HAGF			
HSRA HSRB HSRE	STROMAL - OSTEOCLASTOMA	Uni-ZAP XR	LP03
HSRD HSRF HSRG HSRH	Human Osteoclastoma Stromal Cells - unamplified	Uni-ZAP XR	LP03
HSQA HSQB HSQC HSQD HSQE HSQF HSQG	Stromal cell TF274	Uni-ZAP XR	LP03
HSKA HSKB HSKC HSKD HSKF HSKZ	Smooth muscle, serum treated	Uni-ZAP XR	LP03
HSLA HSLB HSLC HSLD HSLF HSLG	Smooth muscle, control	Uni-ZAP XR	LP03
HSDA HSDD HSDE HSDF HSDG HSDH	Spinal cord	Uni-ZAP XR	LP03
HPWS	Prostate-BPH subtracted II	pBS	LP03
HSKW HSKX HSKY	Smooth Muscle- HASTE normalized	pBS	LP03
HFPB HFPC HFPD	H. Frontal cortex, epileptic; re-excision	Uni-ZAP XR	LP03
HSDI HSDJ HSDK	Spinal Cord, re-excision	Uni-ZAP XR	LP03
HSKN HSKO	Smooth Muscle Serum Treated, Norm	pBS	LP03
HSKG HSKH HSKI	Smooth muscle, serum induced, re-exc	pBS	LP03
HFCA HFCB HFCC HFCD HFCE HFCF	Human Fetal Brain	Uni-ZAP XR	LP04
HPTA HPTB HPTD	Human Pituitary	Uni-ZAP XR	LP04
HTHB HTHC HTHD	Human Thymus	Uni-ZAP XR	LP04
HE6B HE6C HE6D HE6E HE6F HE6G HE6S	Human Whole Six Week Old Embryo	Uni-ZAP XR	LP04
HSSA HSSB HSSC HSSD HSSE HSSF HSSG HSSH HSSI HSSJ HSSK	Human Synovial Sarcoma	Uni-ZAP XR	LP04
HE7T	7 Week Old Early Stage Human, subtracted	Uni-ZAP XR	LP04
HEPA HEPB HEPC	Human Epididymus	Uni-ZAP XR	LP04
HSNA HSNB HSNC HSNM HSNM	Human Synovium	Uni-ZAP XR	LP04
HPFB HPFC HPFD HPFE	Human Prostate Cancer, Stage C fraction	Uni-ZAP XR	LP04
HE2A HE2D HE2E HE2H HE2I HE2M HE2N HE2O	12 Week Old Early Stage Human	Uni-ZAP XR	LP04
HE2B HE2C HE2F HE2G HE2P HE2Q	12 Week Old Early Stage Human, II	Uni-ZAP XR	LP04
HPTS HPTT HPTU	Human Pituitary, subtracted	Uni-ZAP XR	LP04
HAUA HAUB HAUC	Amniotic Cells - TNF induced	Uni-ZAP XR	LP04
HAQA HAQB HAQC HAQD	Amniotic Cells - Primary Culture	Uni-ZAP XR	LP04
HWTA HWTB HWTC	wilm's tumor	Uni-ZAP XR	LP04
HBSD	Bone Cancer, re-excision	Uni-ZAP XR	LP04
HSGB	Salivary gland, re-excision	Uni-ZAP XR	LP04

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HSJA HSJB HSJC	Smooth muscle-ILb induced	Uni-ZAP XR	LP04
HSXA HSXB HSXC HSXD	Human Substantia Nigra	Uni-ZAP XR	LP04
HSJA HSJB HSJC	Smooth muscle, IL1b induced	Uni-ZAP XR	LP04
HOUA HOUB HOUC HOUD HOUE	Adipocytes	Uni-ZAP XR	LP04
HPWA HPWB HPWC HPWD HPWE	Prostate BPH	Uni-ZAP XR	LP04
HELA HELB HELC HELD HELE HELF HELG HELH	Endothelial cells-control	Uni-ZAP XR	LP04
HEMA HEMB HEMC HEMD HEME HEMF HEMG HEMH	Endothelial-induced	Uni-ZAP XR	LP04
HBIA HBIB HBIC	Human Brain, Striatum	Uni-ZAP XR	LP04
HHSa HHSB HHSC HHSD HHSE	Human Hypothalamus, Schizophrenia	Uni-ZAP XR	LP04
HNGA HNGB HNGC HNGD HNGE HNGF HNGG HNGH HNGI HNGJ	neutrophils control	Uni-ZAP XR	LP04
HNHA HNHB HNHC HNHD HNHE HNHF HNHG HNHH HNHI HNHI	Neutrophils IL-1 and LPS induced	Uni-ZAP XR	LP04
HSDB HSDC	STRIATUM DEPRESSION	Uni-ZAP XR	LP04
HHPT	Hypothalamus	Uni-ZAP XR	LP04
HSAT HSAU HSAV HSAW HSAX HSAY HSAZ	Anergic T-cell	Uni-ZAP XR	LP04
HBMS HBMT HBMU HBMV HBMW HBMX	Bone marrow	Uni-ZAP XR	LP04
HOEA HOEB HOEC HOED HOEE HOEF HOEJ	Osteoblasts	Uni-ZAP XR	LP04
HAIA HAIB HAIC HAID HAIE HAIF	Epithelial-TNFa and INF induced	Uni-ZAP XR	LP04
HTGA HTGB HTGC HTGD	Apoptotic T-cell	Uni-ZAP XR	LP04
HMCA HMCB HMCC HMCD HMCE	Macrophage-oxLDL	Uni-ZAP XR	LP04
HMAA HMAB HMAc HMAD HMAE HMAF HMAG	Macrophage (GM-CSF treated)	Uni-ZAP XR	LP04
HPHA	Normal Prostate	Uni-ZAP XR	LP04
HPIA HPIB HPIC	LNCAP prostate cell line	Uni-ZAP XR	LP04
HPJA HPJB HPJC	PC3 Prostate cell line	Uni-ZAP XR	LP04
HOSE HOSF HOSG	Human Osteoclastoma, re-excision	Uni-ZAP XR	LP04
HTGE HTGF	Apoptotic T-cell, re-excision	Uni-ZAP XR	LP04
HMAJ HMAK	H Macrophage (GM-CSF treated), re-excision	Uni-ZAP XR	LP04
HACB HACC HACD	Human Adipose Tissue, re-excision	Uni-ZAP XR	LP04
HFPA	H. Frontal Cortex, Epileptic	Uni-ZAP XR	LP04
HFAA HFAB HFAC HFAD HFAE	Alzheimer's, spongy change	Uni-ZAP XR	LP04
HFAM	Frontal Lobe, Dementia	Uni-ZAP XR	LP04
HMIA HMIB HMIC	Human Manic Depression	Uni-ZAP XR	LP04

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
	Tissue		
HTSA HTSE HTSF HTSG HTSH	Human Thymus	pBS	LP05
HPBA HPBB HPBC HPBD HPBE	Human Pineal Gland	pBS	LP05
HSAA HSAB HSAC	HSA 172 Cells	pBS	LP05
HSBA HSBB HSBC HSBM	HSC172 cells	pBS	LP05
HJAA HJAB HJAC HJAD	Jurkat T-cell G1 phase	pBS	LP05
HJBA HJBB HJBC HJBD	Jurkat T-Cell, S phase	pBS	LP05
HAFA HAFB	Aorta endothelial cells + TNF- α	pBS	LP05
HAWA HAWB HAWC	Human White Adipose	pBS	LP05
HTNA HTNB	Human Thyroid	pBS	LP05
HONA	Normal Ovary, Premenopausal	pBS	LP05
HARA HARB	Human Adult Retina	pBS	LP05
HLJA HLJB	Human Lung	pCMVSPORT 1	LP06
HOFM HOFN HOFO	H. Ovarian Tumor, II, OV5232	pCMVSPORT 2.0	LP07
HOGA HOGB HOGC	OV 10-3-95	pCMVSPORT 2.0	LP07
HCGL	CD34+cells, II	pCMVSPORT 2.0	LP07
HDLA	Hodgkin's Lymphoma I	pCMVSPORT 2.0	LP07
HDTA HDTB HDTC HDTD HDTE	Hodgkin's Lymphoma II	pCMVSPORT 2.0	LP07
HKAA HKAB HKAC HKAD HKAE HKAF HKAG HKAH	Keratinocyte	pCMVSPORT2.0	LP07
HCIM	CAPFINDER, Crohn's Disease, lib 2	pCMVSPORT 2.0	LP07
HKAL	Keratinocyte, lib 2	pCMVSPORT2.0	LP07
HKAT	Keratinocyte, lib 3	pCMVSPORT2.0	LP07
HNDA	Nasal polyps	pCMVSPORT2.0	LP07
HDRA	H. Primary Dendritic Cells, lib 3	pCMVSPORT2.0	LP07
HOHA HOHB HOHC	Human Osteoblasts II	pCMVSPORT2.0	LP07
HLDA HLDB HLDC	Liver, Hepatoma	pCMVSPORT3.0	LP08
HLDN HLDO HLDP	Human Liver, normal	pCMVSPORT3.0	LP08
HMTA	pBMC stimulated w/ poly I/C	pCMVSPORT3.0	LP08
HNTA	NTERA2, control	pCMVSPORT3.0	LP08
HDP A HDPB HDPC HDPD HDPF HDPG HDPH HDPI HDPJ HDPK	Primary Dendritic Cells, lib 1	pCMVSPORT3.0	LP08
HDPM HDPN HDPO HDPP	Primary Dendritic cells, frac 2	pCMVSPORT3.0	LP08
HMUA HMUB HMUC	Myeloid Progenitor Cell Line	pCMVSPORT3.0	LP08
HHEA HHEB HHEC HHED	T Cell helper I	pCMVSPORT3.0	LP08
HHEM HHEN HHEO HHEP	T cell helper II	pCMVSPORT3.0	LP08
HEQA HEQB HEQC	Human endometrial stromal cells	pCMVSPORT3.0	LP08
HJMA HJMB	Human endometrial stromal cells-treated with progesterone	pCMVSPORT3.0	LP08
HSWA HSWB HSWC	Human endometrial stromal cells-treated with estradiol	pCMVSPORT3.0	LP08
HSYA HSYB HSYC	Human Thymus Stromal Cells	pCMVSPORT3.0	LP08
HLWA HLWB HLWC	Human Placenta	pCMVSPORT3.0	LP08
HRAA HRAB HRAC	Rejected Kidney, lib 4	pCMVSPORT3.0	LP08

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HMTM	PCR, pBMC I/C treated	PCRII	LP09
HMJA	H. Meningioma, M6	pSport 1	LP10
HMKA HMKB HMKC HMKD HMKE	H. Meningioma, M1	pSport 1	LP10
HUSG HUSI	Human umbilical vein endothelial cells, IL-4 induced	pSport 1	LP10
HUSX HUSY	Human Umbilical Vein Endothelial Cells, uninduced	pSport 1	LP10
HOFA	Ovarian Tumor I, OV5232	pSport 1	LP10
HCFA HCFB HCFC HCFD	T-Cell PHA 16 hrs	pSport 1	LP10
HCFL HCFM HCFN HCFO	T-Cell PHA 24 hrs	pSport 1	LP10
HADA HADC HADD HADE HADF HADG	Human Adipose	pSport 1	LP10
HOVA HOVB HOVC	Human Ovary	pSport 1	LP10
HTWB HTWC HTWD HTWE HTWF	Resting T-Cell Library, II	pSport 1	LP10
HMMA	Spleen metastatic melanoma	pSport 1	LP10
HLYA HLYB HLYC HLYD HLYE	Spleen, Chronic lymphocytic leukemia	pSport 1	LP10
HCGA	CD34+ cell, I	pSport 1	LP10
HEOM HEON	Human Eosinophils	pSport 1	LP10
HTDA	Human Tonsil, Lib 3	pSport 1	LP10
HSPA	Salivary Gland, Lib 2	pSport 1	LP10
HCHA HCHB HCHC	Breast Cancer cell line, MDA 36	pSport 1	LP10
HCHM HCHN	Breast Cancer Cell line, angiogenic	pSport 1	LP10
HCIA	Crohn's Disease	pSport 1	LP10
HDAA HDAB HDAC	HEL cell line	pSport 1	LP10
HABA	Human Astrocyte	pSport 1	LP10
HUFA HUFB HUFC	Ulcerative Colitis	pSport 1	LP10
HNTM	NTERA2 + retinoic acid, 14 days	pSport 1	LP10
HDQA	Primary Dendritic cells, CapFinder2, frac 1	pSport 1	LP10
HDQM	Primary Dendritic Cells, CapFinder, frac 2	pSport 1	LP10
HLDX	Human Liver, normal, CapFinder	pSport 1	LP10
HULA HULB HULC	Human Dermal Endothelial Cells, untreated	pSport 1	LP10
HUMA	Human Dermal Endothelial cells, treated	pSport 1	LP10
HCJA	Human Stromal Endometrial fibroblasts, untreated	pSport 1	LP10
HCJM	Human Stromal endometrial fibroblasts, treated w/ estradiol	pSport 1	LP10
HEDA	Human Stromal endometrial fibroblasts, treated with progesterone	pSport 1	LP10
HFNA	Human ovary tumor cell OV350721	pSport 1	LP10

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HKGA HKGB HKGC HKGD	Merkel Cells	pSport1	LP10
HISA HISB HISC	Pancreas Islet Cell Tumor	pSport1	LP10
HLSA	Skin, burned	pSport1	LP10
HBZA	Prostate, BPH, Lib 2	pSport1	LP10
HBZS	Prostate BPH, Lib 2, subtracted	pSport1	LP10
HFIA HFIB HFIC	Synovial Fibroblasts (control)	pSport1	LP10
HFIH HFII HFIJ	Synovial hypoxia	pSport1	LP10
HFIT HFIU HFIV	Synovial IL-1/TNF stimulated	pSport1	LP10
HGCA	Mesangial cell, frac 1	pSport1	LP10
HMVA HMVB HMVC	Bone Marrow Stromal Cell, untreated	pSport1	LP10
HFIX HFIY HFIZ	Synovial Fibroblasts (III/TNF), subt	pSport1	LP10
HFOX HFOY HFOZ	Synovial hypoxia-RSF subtracted	pSport1	LP10
HMQA HMQB HMQC HMQD	Human Activated Monocytes	Uni-ZAP XR	LP11
HLIA HLIB HLIC	Human Liver	pCMVSPORT 1	LP012
HHBA HHBB HHBC HHBD HHBE	Human Heart	pCMVSPORT 1	LP012
HBBA HBBB	Human Brain	pCMVSPORT 1	LP012
HLJA HLJB HLJC HLJD HLJE	Human Lung	pCMVSPORT 1	LP012
HOGA HOGB HOGC	Ovarian Tumor	pCMVSPORT 2.0	LP012
HTJM	Human Tonsils, Lib 2	pCMVSPORT 2.0	LP012
HAMF HAMG	KMH2	pCMVSPORT 3.0	LP012
HAJA HAJB HAJC	L428	pCMVSPORT 3.0	LP012
HWBA HWBB HWBC HWBD HWBE	Dendritic cells, pooled	pCMVSPORT 3.0	LP012
HWAA HWAB HWAC HWAD HWAE	Human Bone Marrow, treated	pCMVSPORT 3.0	LP012
HYAA HYAB HYAC	B Cell lymphoma	pCMVSPORT 3.0	LP012
HWHG HWHH HWHI	Healing groin wound, 6.5 hours post incision	pCMVSPORT 3.0	LP012
HWHP HWHQ HWHR	Healing groin wound; 7.5 hours post incision	pCMVSPORT 3.0	LP012
HARM	Healing groin wound - zero hr post-incision (control)	pCMVSPORT 3.0	LP012
HBIM	Olfactory epithelium; nasal cavity	pCMVSPORT 3.0	LP012
HWDA	Healing Abdomen wound; 70&90 min post incision	pCMVSPORT 3.0	LP012
HWEA	Healing Abdomen Wound; 15 days post incision	pCMVSPORT 3.0	LP012
HWJA	Healing Abdomen Wound; 21&29 days	pCMVSPORT 3.0	LP012
HNAL	Human Tongue, frac 2	pSport1	LP012
HMJA	H. Meningioma, M6	pSport1	LP012
HMKA HMKB HMKC HMKD HMKE	H. Meningioma, M1	pSport1	LP012
HOFA	Ovarian Tumor I, OV5232	pSport1	LP012
HCFA HCFB HCFC HCFD	T-Cell PHA 16 hrs	pSport1	LP012

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HCFL HCFM HCFN HCFO	T-Cell PHA 24 hrs	pSport1	LP012
HMMA HMMB HMMC	Spleen metastatic melanoma	pSport1	LP012
HTDA	Human Tonsil, Lib 3	pSport1	LP012
HDBA	Human Fetal Thymus	pSport1	LP012
HDLA	Pericardium	pSport1	LP012
HBZA	Prostate, BPH, Lib 2	pSport1	LP012
HWCA	Larynx tumor	pSport1	LP012
HWKA	Normal lung	pSport1	LP012
HSMB	Bone marrow stroma, treated	pSport1	LP012
HBHM	Normal trachea	pSport1	LP012
HLFC	Human Larynx	pSport1	LP012
HLRB	Siebben Polyposis	pSport1	LP012
HNIA	Mammary Gland	pSport1	LP012
HNJB	Palate carcinoma	pSport1	LP012
HNKA	Palate normal	pSport1	LP012
HMZA	Pharynx carcinoma	pSport1	LP012
HABG	Cheek Carcinoma	pSport1	LP012
HMZM	Pharynx Carcinoma	pSport1	LP012
HDRM	Larynx Carcinoma	pSport1	LP012
HVAA	Pancreas normal PCA4 No	pSport1	LP012
HICA	Tongue carcinoma	pSport1	LP012
HUKA HUKB HUKC HUKD HUKE	Human Uterine Cancer	Lambda ZAP II	LP013
HFFA	Human Fetal Brain, random primed	Lambda ZAP II	LP013
HTUA	Activated T-cell labeled with 4-thioluri	Lambda ZAP II	LP013
HBQA	Early Stage Human Brain, random primed	Lambda ZAP II	LP013
HMEB	Human microvascular Endothelial cells, fract. B	Lambda ZAP II	LP013
HUSH	Human Umbilical Vein Endothelial cells, fract. A, re-excision	Lambda ZAP II	LP013
HLQC HLQD	Hepatocellular tumor, re-excision	Lambda ZAP II	LP013
HTWJ HTWK HTWL	Resting T-cell, re-excision	Lambda ZAP II	LP013
HF6S	Human Whole 6 week Old Embryo (II), subt	pBluescript	LP013
HHPs	Human Hippocampus, subtracted	pBluescript	LP013
HL1S	LNCAP, differential expression	pBluescript	LP013
HLHS HLHT	Early Stage Human Lung, Subtracted	pBluescript	LP013
HSUS	Supt cells, cyclohexamide treated, subtracted	pBluescript	LP013
HSUT	Supt cells, cyclohexamide treated, differentially expressed	pBluescript	LP013
HSDS	H. Striatum Depression, subtracted	pBluescript	LP013

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HPTZ	Human Pituitary, Subtracted VII	pBluescript	LP013
HSDX	H. Striatum Depression, subt II	pBluescript	LP013
HSDZ	H. Striatum Depression, subt	pBluescript	LP013
HPBA HPBB HPBC HPBD HPBE	Human Pineal Gland	pBluescript SK-	LP013
HRTA	Colorectal Tumor	pBluescript SK-	LP013
HSBA HSBB HSBC HSBM	HSC172 cells	pBluescript SK-	LP013
HJAA HJAB HJAC HJAD	Jurkat T-cell G1 phase	pBluescript SK-	LP013
HJBA HJBB HJBC HJBD	Jurkat T-cell, S1 phase	pBluescript SK-	LP013
HTNA HTNB	Human Thyroid	pBluescript SK-	LP013
HAHA HAHB	Human Adult Heart	Uni-ZAP XR	LP013
HE6A	Whole 6 week Old Embryo	Uni-ZAP XR	LP013
HFCA HFCE HFCC HFCD HFCE	Human Fetal Brain	Uni-ZAP XR	LP013
HFKE HFKE HFKE HFKE HFKE	Human Fetal Kidney	Uni-ZAP XR	LP013
HGBA HGBD HGBE HGBF HGBG	Human Gall Bladder	Uni-ZAP XR	LP013
HPRB HPRB HPRC HPRD	Human Prostate	Uni-ZAP XR	LP013
HTEA HTEB HTEC HTED HTEE	Human Testes	Uni-ZAP XR	LP013
HTTA HTTB HTTC HTTD HTTE	Human Testes Tumor	Uni-ZAP XR	LP013
HYBA HYBB	Human Fetal Bone	Uni-ZAP XR	LP013
HFLA	Human Fetal Liver	Uni-ZAP XR	LP013
HHFB HHFC HHFD HHFE HHFF	Human Fetal Heart	Uni-ZAP XR	LP013
HUVB HUVB HUVB HUVB	Human Umbilical Vein, End. remake	Uni-ZAP XR	LP013
HTHB HTHC HTHD	Human Thymus	Uni-ZAP XR	LP013
HSTA HSTB HSTC HSTD	Human Skin Tumor	Uni-ZAP XR	LP013
HTAA HTAB HTAC HTAD HTAE	Human Activated T-cells	Uni-ZAP XR	LP013
HFEA HFEB HFEC	Human Fetal Epithelium (skin)	Uni-ZAP XR	LP013
HJPA HJPB HJPC HJPD	Human Jurkat Membrane Bound Polysomes	Uni-ZAP XR	LP013
HESA	Human Epithelioid Sarcoma	Uni-ZAP XR	LP013
HALS	Human Adult Liver, Subtracted	Uni-ZAP XR	LP013
HFTA HFTB HFTC HFTD	Human Fetal Dura Mater	Uni-ZAP XR	LP013
HCAA HCAB HCAC	Cem cells, cyclohexamide treated	Uni-ZAP XR	LP013
HRGA HRGB HRGC HRGD	Raji Cells, cyclohexamide treated	Uni-ZAP XR	LP013
HE9A HE9B HE9C HE9D HE9E	Nine Week Old Early Stage Human	Uni-ZAP XR	LP013
HSFA	Human Fibrosarcoma	Uni-ZAP XR	LP013
HATA HATB HATC HATD HATE	Human Adrenal Gland Tumor	Uni-ZAP XR	LP013
HTRA	Human Trachea Tumor	Uni-ZAP XR	LP013
HE2A HE2D HE2E HE2H HE2I	12 Week Old Early Stage	Uni-ZAP XR	LP013

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
	Human		
HE2B HE2C HE2F HE2G HE2P	12 Week Old Early Stage Human, II	Uni-ZAP XR	LP013
HNEA HNEB HNEC HNED HNEE	Human Neutrophil	Uni-ZAP XR	LP013
HBGA	Human Primary Breast Cancer	Uni-ZAP XR	LP013
HPTS HPTT HPTU	Human Pituitary, subtracted	Uni-ZAP XR	LP013
HMQA HMQB HMQC HMQD	Human Activated Monocytes	Uni-ZAP XR	LP013
HOAA HOAB HOAC	Human Osteosarcoma	Uni-ZAP XR	LP013
HTOA HTOD HTOE HTOF HTOG	human tonsils	Uni-ZAP XR	LP013
HMGB	Human OB MG63 control fraction I	Uni-ZAP XR	LP013
HOPB	Human OB HOS control fraction I	Uni-ZAP XR	LP013
HOQB	Human OB HOS treated (1 nM E2) fraction I	Uni-ZAP XR	LP013
HAUA HAUB HAUC	Amniotic Cells - TNF induced	Uni-ZAP XR	LP013
HAQA HAQB HAQC HAQD	Amniotic Cells - Primary Culture	Uni-ZAP XR	LP013
HROA HROC	HUMAN STOMACH	Uni-ZAP XR	LP013
HBJA HBJB HBJC HBJD HBJE	HUMAN B CELL LYMPHOMA	Uni-ZAP XR	LP013
HODA HODB HODC HODD	human ovarian cancer	Uni-ZAP XR	LP013
HCPA	Corpus Callosum	Uni-ZAP XR	LP013
HSOA	stomach cancer (human)	Uni-ZAP XR	LP013
HERA	SKIN	Uni-ZAP XR	LP013
HMDA	Brain-medulloblastoma	Uni-ZAP XR	LP013
HGLA HGLB HGLD	Glioblastoma	Uni-ZAP XR	LP013
HWTA HWTB HWTC	wilm's tumor	Uni-ZAP XR	LP013
HEAA	H. Atrophic Endometrium	Uni-ZAP XR	LP013
HAPN HAPO HAPP HAPQ HAPR	Human Adult Pulmonary;re-excision	Uni-ZAP XR	LP013
HLTG HLTH	Human T-cell lymphoma;re-excision	Uni-ZAP XR	LP013
HAHC HAHD HAHE	Human Adult Heart;re-excision	Uni-ZAP XR	LP013
HAGA HAGB HAGC HAGD HAGE	Human Amygdala	Uni-ZAP XR	LP013
HSJA HSJB HSJC	Smooth muscle-ILb induced	Uni-ZAP XR	LP013
SHSA HSHB HSHC	Smooth muscle, IL1b induced	Uni-ZAP XR	LP013
HPWA HPWB HPWC HPWD HPWE	Prostate BPH	Uni-ZAP XR	LP013
HPIA HPIB HPIC	LNCAP prostate cell line	Uni-ZAP XR	LP013
HPJA HPJB HPJC	PC3 Prostate cell line	Uni-ZAP XR	LP013
HBTA	Bone Marrow Stroma, TNF&LPS ind	Uni-ZAP XR	LP013
HMCF HMCG HMCH HMCJ	Macrophage-oxLDL; re-excision	Uni-ZAP XR	LP013
HAGG HAGH HAGI	Human Amygdala;re-excision	Uni-ZAP XR	LP013
HACA	H. Adipose Tissue	Uni-ZAP XR	LP013

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HKFB	K562 + PMA (36 hrs),re-excision	ZAP Express	LP013
HCWT HCWU HCWV	CD34 positive cells (cord blood),re-ex	ZAP Express	LP013
HBWA	Whole brain	ZAP Express	LP013
HBXA HBXB HBXC HBXD	Human Whole Brain #2 - Oligo dT > 1.5Kb	ZAP Express	LP013
HAVM	Temporal cortex-Alzheimer	pT-Adv	LP014
HAVT	Hippocampus, Alzheimer Subtracted	pT-Adv	LP014
HHAS	CHME Cell Line	Uni-ZAP XR	LP014
HAJR	Larynx normal	pSport 1	LP014
HWLE HWLF HWLG HWLH	Colon Normal	pSport 1	LP014
HCRM HCRN HCRO	Colon Carcinoma	pSport 1	LP014
HWLI HWLJ HWLK	Colon Normal	pSport 1	LP014
HWLQ HWLR HWLS HWLT	Colon Tumor	pSport 1	LP014
HBFM	Gastrocnemius Muscle	pSport 1	LP014
HBOD HBOE	Quadriceps Muscle	pSport 1	LP014
HBKD HBKE	Soleus Muscle	pSport 1	LP014
HCCM	Pancreatic Langerhans	pSport 1	LP014
HWGA	Larynx carcinoma	pSport 1	LP014
HWGM HWGN	Larynx carcinoma	pSport 1	LP014
HWLA HWLB HWLC	Normal colon	pSport 1	LP014
HWLM HWLN	Colon Tumor	pSport 1	LP014
HVAM HVAN HVAO	Pancreas Tumor	pSport 1	LP014
HWGQ	Larynx carcinoma	pSport 1	LP014
HAQM HAQN	Salivary Gland	pSport 1	LP014
HASM	Stomach; normal	pSport 1	LP014
HBCM	Uterus; normal	pSport 1	LP014
HCDM	Testis; normal	pSport 1	LP014
HDJM	Brain; normal	pSport 1	LP014
HEFM	Adrenal Gland,normal	pSport 1	LP014
HBAA	Rectum normal	pSport 1	LP014
HFDm	Rectum tumour	pSport 1	LP014
HGAM	Colon, normal	pSport 1	LP014
HHMM	Colon, tumour	pSport 1	LP014
HCLB HCLC	Human Lung Cancer	Lambda Zap II	LP015
HRLA	L1 Cell line	ZAP Express	LP015
HHAM	Hypothalamus, Alzheimer's	pCMVSPORT 3.0	LP015
HKBA	Ku 812F Basophils Line	pSport 1	LP015
HS2S	Saos2, Dexamethosone Treated	pSport 1	LP016
HA5A	Lung Carcinoma A549 TNFalpha activated	pSport 1	LP016
HTFM	TF-1 Cell Line GM-CSF Treated	pSport 1	LP016
HYAS	Thyroid Tumour	pSport 1	LP016
HUTS	Larynx Normal	pSport 1	LP016
HXOA	Larynx Tumor	pSport 1	LP016
HEAH	Ea.hy.926 cell line	pSport 1	LP016
HINA	Adenocarcinoma Human	pSport 1	LP016
HRMA	Lung Mesothelium	pSport 1	LP016

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HLCL	Human Pre-Differentiated Adipocytes	Uni-Zap XR	LP017
HS2A	Saos2 Cells	pSport 1	LP020
HS2I	Saos2 Cells; Vitamin D3 Treated	pSport 1	LP020
HUCM	CHME Cell Line, untreated	pSport 1	LP020
HEPN	Aryepiglottis Normal	pSport 1	LP020
HPSN	Sinus Piniformis Tumour	pSport 1	LP020
HNSA	Stomach Normal	pSport 1	LP020
HNSM	Stomach Tumour	pSport 1	LP020
HNLA	Liver Normal Met5No	pSport 1	LP020
HUTA	Liver Tumour Met 5 Tu	pSport 1	LP020
HOCN	Colon Normal	pSport 1	LP020
HOCT	Colon Tumor	pSport 1	LP020
HTNT	Tongue Tumour	pSport 1	LP020
HLXN	Larynx Normal	pSport 1	LP020
HLXT	Larynx Tumour	pSport 1	LP020
HTYN	Thymus	pSport 1	LP020
HPLN	Placenta	pSport 1	LP020
HTNG	Tongue Normal	pSport 1	LP020
HZAA	Thyroid Normal (SDCA2 No)	pSport 1	LP020
HWES	Thyroid Thyroiditis	pSport 1	LP020
HFHD	Ficoll Human Stromal Cells, 5Fu treated	pTrip1Ex2	LP021
HFHM, HFHN	Ficoll Human Stromal Cells, Untreated	pTrip1Ex2	LP021
HPCI	Hep G2 Cells, lambda library	lambda Zap-CMV XR	LP021
HBCA, HBCB, HBCC	H. Lymph node breast Cancer	Uni-ZAP XR	LP021
HCOK	Chondrocytes	pSPORT1	LP022
HDCA, HDCB, HDCC	Dendritic Cells From CD34 Cells	pSPORT1	LP022
HDMA, HDMB	CD40 activated monocyte dendritic cells	pSPORT1	LP022
HDDM, HDDN, HDDO	LPS activated derived dendritic cells	pSPORT1	LP022
HPCR	Hep G2 Cells, PCR library	lambda Zap-CMV XR	LP022
HAAA, HAAB, HAAC	Lung, Cancer (4005313A3): Invasive Poorly Differentiated Lung Adenocarcinoma	pSPORT1	LP022
HIPA, HIPB, HIPC	Lung, Cancer (4005163 B7): Invasive, Poorly Diff. Adenocarcinoma, Metastatic	pSPORT1	LP022
HOOH, HOOI	Ovary, Cancer: (4004562 B6) Papillary Serous Cystic Neoplasm, Low Malignant Pot	pSPORT1	LP022
HIDA	Lung, Normal: (4005313 B1)	pSPORT1	LP022
HUJA, HUJB, HUJC, HUJD, HUIE	B-Cells	pCMVSPORT 3.0	LP022
HNOA, HNOB, HNOC, HNOD	Ovary, Normal: (9805C040R)	pSPORT1	LP022

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HNLM	Lung, Normal: (4005313 B1)	pSPORT1	LP022
HSCL	Stromal Cells	pSPORT1	LP022
HAAX	Lung, Cancer: (4005313 A3) Invasive Poorly-differentiated Metastatic lung adenocarcinoma	pSPORT1	LP022
HUUA,HUUB,HUUC,HUUD	B-cells (unstimulated)	pTrip1Ex2	LP022
HWWA,HWWB,HWWC,HWW D,HWWE,HWWF,HWWG	B-cells (stimulated)	pSPORT1	LP022
HCCC	Colon, Cancer: (9808C064R)	pCMVSport 3.0	LP023
HPDO HPDP HPDQ HPDR HPD	Ovary, Cancer (9809C332): Poorly differentiated adenocarcinoma	pSport 1	LP023
HPCO HPCP HPCQ HPCT	Ovary, Cancer (15395A1F): Grade II Papillary Carcinoma	pSport 1	LP023
HOCM HOCO HOCQ HOCQ	Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma	pSport 1	LP023
HCBM HCBN HCBO	Breast, Cancer: (4004943 A5)	pSport 1	LP023
HNBT HNBU HNBV	Breast, Normal: (4005522B2)	pSport 1	LP023
HBCP HBCQ	Breast, Cancer: (4005522 A2)	pSport 1	LP023
HBCJ	Breast, Cancer: (9806C012R)	pSport 1	LP023
HSAM HSAN	Stromal cells 3.88	pSport 1	LP023
HVCA HVCB HVCC HVCD	Ovary, Cancer: (4004332 A2)	pSport 1	LP023
HSCK HSEN HSEO	Stromal cells (HBM3.18)	pSport 1	LP023
HSCP HSCQ	stromal cell clone 2.5	pSport 1	LP023
HUXA	Breast Cancer: (4005385 A2)	pSport 1	LP023
HCOM HCON HCOO HCOP HCOQ	Ovary, Cancer (4004650 A3): Well-Differentiated Micropapillary Serous Carcinoma	pSport 1	LP023
HBNM	Breast, Cancer: (9802C020E)	pSport 1	LP023
HVVA HVVB HVVC HVVD HVVE	Human Bone Marrow, treated	pSport 1	LP023

Two nonlimiting examples are provided below for isolating a particular clone from the deposited sample of plasmid cDNAs cited for that clone in Table 7. First, a plasmid is directly isolated by screening the clones using a polynucleotide probe corresponding to the nucleotide sequence of SEQ ID NO:X.

Particularly, a specific polynucleotide with 30-40 nucleotides is synthesized using an Applied Biosystems DNA synthesizer according to the sequence reported. The oligonucleotide is labeled, for instance, with ^{32}P - γ -ATP using T4 polynucleotide kinase and purified according to routine methods. (E.g., Maniatis et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring, NY (1982)). The plasmid mixture is transformed into a suitable host, as indicated above (such as XL-1 Blue (Stratagene)) using techniques known to those of skill in the art, such as those provided by the vector supplier or in related publications or patents cited above. The transformants are plated on 1.5% agar plates (containing the appropriate selection

agent, e.g., ampicillin) to a density of about 150 transformants (colonies) per plate. These plates are screened using Nylon membranes according to routine methods for bacterial colony screening (e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Edit., (1989), Cold Spring Harbor Laboratory Press, pages 1.93 to 1.104), or other techniques known to those of skill in the art.

Alternatively, two primers of 17-20 nucleotides derived from both ends of the nucleotide sequence of SEQ ID NO:X are synthesized and used to amplify the desired cDNA using the deposited cDNA plasmid as a template. The polymerase chain reaction is carried out under routine conditions, for instance, in 25 μ l of reaction mixture with 0.5 μ g of the above cDNA template. A convenient reaction mixture is 1.5-5 mM $MgCl_2$, 0.01% (w/v) gelatin, 20 μ M each of dATP, dCTP, dGTP, dTTP, 25 pmol of each primer and 0.25 Unit of Taq polymerase. Thirty five cycles of PCR (denaturation at 94°C for 1 min; annealing at 55°C for 1 min; elongation at 72°C for 1 min) are performed with a Perkin-Elmer Cetus automated thermal cycler. The amplified product is analyzed by agarose gel electrophoresis and the DNA band with expected molecular weight is excised and purified. The PCR product is verified to be the selected sequence by subcloning and sequencing the DNA product.

Several methods are available for the identification of the 5' or 3' non-coding portions of a gene which may not be present in the deposited clone. These methods include but are not limited to, filter probing, clone enrichment using specific probes, and protocols similar or identical to 5' and 3' "RACE" protocols which are well known in the art. For instance, a method similar to 5' RACE is available for generating the missing 5' end of a desired full-length transcript. (Fromont-Racine et al., *Nucleic Acids Res.* 21(7):1683-1684 (1993)).

Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcripts. A primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest is used to PCR amplify the 5' portion of the desired full-length gene. This amplified product may then be sequenced and used to generate the full length gene.

This above method starts with total RNA isolated from the desired source, although poly-A+ RNA can be used. The RNA preparation can then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase should then be inactivated and the RNA treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase.

This modified RNA preparation is used as a template for first strand cDNA synthesis using a gene specific oligonucleotide. The first strand synthesis reaction is used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide

and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the desired gene.

Example 2: Isolation of Genomic Clones Corresponding to a Polynucleotide

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A human genomic P1 library (Genomic Systems, Inc.) is screened by PCR using primers selected for the sequence corresponding to SEQ ID NO:X according to the method described in Example 1. (See also, Sambrook.)

10

Example 3: Tissue specific expression analysis

The Human Genome Sciences, Inc. (HGS) database is derived from sequencing tissue and/or disease specific cDNA libraries. Libraries generated from a particular tissue are selected and the specific tissue expression pattern of EST groups or assembled contigs within these
15 libraries is determined by comparison of the expression patterns of those groups or contigs within the entire database. ESTs and assembled contigs which show tissue specific expression are selected.

The original clone from which the specific EST sequence was generated, or in the case of an assembled contig, the clone from which the 5' most EST sequence was generated, is obtained
20 from the catalogued library of clones and the insert amplified by PCR using methods known in the art. The PCR product is denatured and then transferred in 96 or 384 well format to a nylon membrane (Schleicher and Scheull) generating an array filter of tissue specific clones. Housekeeping genes, maize genes, and known tissue specific genes are included on the filters. These targets can be used in signal normalization and to validate assay sensitivity. Additional
25 targets are included to monitor probe length and specificity of hybridization.

Radioactively labeled hybridization probes are generated by first strand cDNA synthesis per the manufacturer's instructions (Life Technologies) from mRNA/RNA samples prepared from the specific tissue being analyzed (e.g., prostate, prostate cancer, ovarian, ovarian cancer, etc.). The hybridization probes are purified by gel exclusion chromatography, quantitated, and
30 hybridized with the array filters in hybridization bottles at 65°C overnight. The filters are washed under stringent conditions and signals are captured using a Fuji phosphorimager.

Data is extracted using AIS software and following background subtraction, signal normalization is performed. This includes a normalization of filter-wide expression levels between different experimental runs. Genes that are differentially expressed in the tissue of interest are
35 identified.

Example 4: Chromosomal Mapping of the Polynucleotides

An oligonucleotide primer set is designed according to the sequence at the 5' end of SEQ ID NO:X. This primer preferably spans about 100 nucleotides. This primer set is then used in a polymerase chain reaction under the following set of conditions: 30 seconds, 95°C; 1 minute, 56°C; 1 minute, 70°C. This cycle is repeated 32 times followed by one 5 minute cycle at 70°C. Human, mouse, and hamster DNA is used as template in addition to a somatic cell hybrid panel containing individual chromosomes or chromosome fragments (Bios, Inc). The reactions are analyzed on either 8% polyacrylamide gels or 3.5 % agarose gels. Chromosome mapping is determined by the presence of an approximately 100 bp PCR fragment in the particular somatic cell hybrid.

Example 5: Bacterial Expression of a Polypeptide

A polynucleotide encoding a polypeptide of the present invention is amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence, as outlined in Example 1, to synthesize insertion fragments. The primers used to amplify the cDNA insert should preferably contain restriction sites, such as BamHI and XbaI, at the 5' end of the primers in order to clone the amplified product into the expression vector. For example, BamHI and XbaI correspond to the restriction enzyme sites on the bacterial expression vector pQE-9. (Qiagen, Inc., Chatsworth, CA). This plasmid vector encodes antibiotic resistance (Amp^r), a bacterial origin of replication (ori), an IPTG-regulatable promoter/operator (P/O), a ribosome binding site (RBS), a 6-histidine tag (6-His), and restriction enzyme cloning sites.

The pQE-9 vector is digested with BamHI and XbaI and the amplified fragment is ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial RBS. The ligation mixture is then used to transform the E. coli strain M15/rep4 (Qiagen, Inc.) which contains multiple copies of the plasmid pREP4, which expresses the lacI repressor and also confers kanamycin resistance (Kan^r). Transformants are identified by their ability to grow on LB plates and ampicillin/kanamycin resistant colonies are selected. Plasmid DNA is isolated and confirmed by restriction analysis.

Clones containing the desired constructs are grown overnight (O/N) in liquid culture in LB media supplemented with both Amp (100 ug/ml) and Kan (25 ug/ml). The O/N culture is used to inoculate a large culture at a ratio of 1:100 to 1:250. The cells are grown to an optical density 600 (O.D.⁶⁰⁰) of between 0.4 and 0.6. IPTG (Isopropyl-B-D-thiogalacto pyranoside) is then added to a final concentration of 1 mM. IPTG induces by inactivating the lacI repressor, clearing the P/O leading to increased gene expression.

Cells are grown for an extra 3 to 4 hours. Cells are then harvested by centrifugation (20 mins at 6000Xg). The cell pellet is solubilized in the chaotropic agent 6 Molar Guanidine HCl by stirring for 3-4 hours at 4°C. The cell debris is removed by centrifugation, and the supernatant containing the polypeptide is loaded onto a nickel-nitrilo-tri-acetic acid ("Ni-NTA") affinity resin column (available from QIAGEN, Inc., *supra*). Proteins with a 6 x His tag bind to the Ni-NTA resin with high affinity and can be purified in a simple one-step procedure (for details see: The QIAexpressionist (1995) QIAGEN, Inc., *supra*).

Briefly, the supernatant is loaded onto the column in 6 M guanidine-HCl, pH 8. The column is first washed with 10 volumes of 6 M guanidine-HCl, pH 8, then washed with 10 volumes of 6 M guanidine-HCl pH 6, and finally the polypeptide is eluted with 6 M guanidine-HCl, pH 5.

The purified protein is then renatured by dialyzing it against phosphate-buffered saline (PBS) or 50 mM Na-acetate, pH 6 buffer plus 200 mM NaCl. Alternatively, the protein can be successfully refolded while immobilized on the Ni-NTA column. The recommended conditions are as follows: renature using a linear 6M-1M urea gradient in 500 mM NaCl, 20% glycerol, 20 mM Tris/HCl pH 7.4, containing protease inhibitors. The renaturation should be performed over a period of 1.5 hours or more. After renaturation the proteins are eluted by the addition of 250 mM imidazole. Imidazole is removed by a final dialyzing step against PBS or 50 mM sodium acetate pH 6 buffer plus 200 mM NaCl. The purified protein is stored at 4°C or frozen at -80°C.

In addition to the above expression vector, the present invention further includes an expression vector, called pHE4a (ATCC Accession Number 209645, deposited on February 25, 1998) which contains phage operator and promoter elements operatively linked to a polynucleotide of the present invention, called pHE4a. (ATCC Accession Number 209645, deposited on February 25, 1998.) This vector contains: 1) a neomycinphosphotransferase gene as a selection marker, 2) an E. coli origin of replication, 3) a T5 phage promoter sequence, 4) two lac operator sequences, 5) a Shine-Delgarno sequence, and 6) the lactose operon repressor gene (*lacIq*). The origin of replication (*oriC*) is derived from pUC19 (LTI, Gaithersburg, MD). The promoter and operator sequences are made synthetically.

DNA can be inserted into the pHE4a by restricting the vector with NdeI and XbaI, BamHI, XhoI, or Asp718, running the restricted product on a gel, and isolating the larger fragment (the stuffer fragment should be about 310 base pairs). The DNA insert is generated according to the PCR protocol described in Example 1, using PCR primers having restriction sites for NdeI (5' primer) and XbaI, BamHI, XhoI, or Asp718 (3' primer). The PCR insert is gel purified and restricted with compatible enzymes. The insert and vector are ligated according to standard protocols.

The engineered vector could easily be substituted in the above protocol to express protein in a bacterial system.

Example 6: Purification of a Polypeptide from an Inclusion Body

The following alternative method can be used to purify a polypeptide expressed in *E. coli* when it is present in the form of inclusion bodies. Unless otherwise specified, all of the following steps are conducted at 4-10°C.

Upon completion of the production phase of the *E. coli* fermentation, the cell culture is cooled to 4-10°C and the cells harvested by continuous centrifugation at 15,000 rpm (Heraeus Sepatech). On the basis of the expected yield of protein per unit weight of cell paste and the amount of purified protein required, an appropriate amount of cell paste, by weight, is suspended in a buffer solution containing 100 mM Tris, 50 mM EDTA, pH 7.4. The cells are dispersed to a homogeneous suspension using a high shear mixer.

The cells are then lysed by passing the solution through a microfluidizer (Microfluidics, Corp. or APV Gaulin, Inc.) twice at 4000-6000 psi. The homogenate is then mixed with NaCl solution to a final concentration of 0.5 M NaCl, followed by centrifugation at 7000 xg for 15 min. The resultant pellet is washed again using 0.5M NaCl, 100 mM Tris, 50 mM EDTA, pH 7.4.

The resulting washed inclusion bodies are solubilized with 1.5 M guanidine hydrochloride (GuHCl) for 2-4 hours. After 7000 xg centrifugation for 15 min., the pellet is discarded and the polypeptide containing supernatant is incubated at 4°C overnight to allow further GuHCl extraction.

Following high speed centrifugation (30,000 xg) to remove insoluble particles, the GuHCl solubilized protein is refolded by quickly mixing the GuHCl extract with 20 volumes of buffer containing 50 mM sodium, pH 4.5, 150 mM NaCl, 2 mM EDTA by vigorous stirring. The refolded diluted protein solution is kept at 4°C without mixing for 12 hours prior to further purification steps.

To clarify the refolded polypeptide solution, a previously prepared tangential filtration unit equipped with 0.16 µm membrane filter with appropriate surface area (e.g., Filtron), equilibrated with 40 mM sodium acetate, pH 6.0 is employed. The filtered sample is loaded onto a cation exchange resin (e.g., Poros HS-50, Perseptive Biosystems). The column is washed with 40 mM sodium acetate, pH 6.0 and eluted with 250 mM, 500 mM, 1000 mM, and 1500 mM NaCl in the same buffer, in a stepwise manner. The absorbance at 280 nm of the effluent is continuously monitored. Fractions are collected and further analyzed by SDS-PAGE.

Fractions containing the polypeptide are then pooled and mixed with 4 volumes of water. The diluted sample is then loaded onto a previously prepared set of tandem columns of strong anion (Poros HQ-50, Perseptive Biosystems) and weak anion (Poros CM-20, Perseptive Biosystems) exchange resins. The columns are equilibrated with 40 mM sodium acetate, pH 6.0.

Both columns are washed with 40 mM sodium acetate, pH 6.0, 200 mM NaCl. The CM-20 column is then eluted using a 10 column volume linear gradient ranging from 0.2 M NaCl, 50 mM sodium acetate, pH 6.0 to 1.0 M NaCl, 50 mM sodium acetate, pH 6.5. Fractions are collected under constant A₂₈₀ monitoring of the effluent. Fractions containing the polypeptide (determined, for instance, by 16% SDS-PAGE) are then pooled.

The resultant polypeptide should exhibit greater than 95% purity after the above refolding and purification steps. No major contaminant bands should be observed from Commassie blue stained 16% SDS-PAGE gel when 5 µg of purified protein is loaded. The purified protein can also be tested for endotoxin/LPS contamination, and typically the LPS content is less than 0.1 ng/ml according to LAL assays.

Example 7: Cloning and Expression of a Polypeptide in a Baculovirus Expression System

In this example, the plasmid shuttle vector pA2 is used to insert a polynucleotide into a baculovirus to express a polypeptide. This expression vector contains the strong polyhedrin promoter of the *Autographa californica* nuclear polyhedrosis virus (AcMNPV) followed by convenient restriction sites such as BamHI, Xba I and Asp718. The polyadenylation site of the simian virus 40 ("SV40") is used for efficient polyadenylation. For easy selection of recombinant virus, the plasmid contains the beta-galactosidase gene from *E. coli* under control of a weak *Drosophila* promoter in the same orientation, followed by the polyadenylation signal of the polyhedrin gene. The inserted genes are flanked on both sides by viral sequences for cell-mediated homologous recombination with wild-type viral DNA to generate a viable virus that express the cloned polynucleotide.

Many other baculovirus vectors can be used in place of the vector above, such as pAc373, pVL941, and pAcIM1, as one skilled in the art would readily appreciate, as long as the construct provides appropriately located signals for transcription, translation, secretion and the like, including a signal peptide and an in-frame AUG as required. Such vectors are described, for instance, in Luckow et al., *Virology* 170:31-39 (1989).

Specifically, the cDNA sequence contained in the deposited clone, including the AUG initiation codon, is amplified using the PCR protocol described in Example 1. If a naturally occurring signal sequence is used to produce the polypeptide of the present invention, the pA2 vector does not need a second signal peptide. Alternatively, the vector can be modified (pA2 GP) to include a baculovirus leader sequence, using the standard methods described in Summers et al., "A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures," Texas Agricultural Experimental Station Bulletin No. 1555 (1987).

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("GeneClean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

5 The plasmid is digested with the corresponding restriction enzymes and optionally, can be dephosphorylated using calf intestinal phosphatase, using routine procedures known in the art. The DNA is then isolated from a 1% agarose gel using a commercially available kit ("GeneClean" BIO 101 Inc., La Jolla, Ca.).

10 The fragment and the dephosphorylated plasmid are ligated together with T4 DNA ligase. *E. coli* HB101 or other suitable *E. coli* hosts such as XL-1 Blue (Stratagene Cloning Systems, La Jolla, CA) cells are transformed with the ligation mixture and spread on culture plates. Bacteria containing the plasmid are identified by digesting DNA from individual colonies and analyzing the digestion product by gel electrophoresis. The sequence of the cloned fragment is confirmed by DNA sequencing.

15 Five μ g of a plasmid containing the polynucleotide is co-transfected with 1.0 μ g of a commercially available linearized baculovirus DNA ("BaculoGold™ baculovirus DNA, Pharmingen, San Diego, CA), using the lipofection method described by Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417 (1987). One μ g of BaculoGold™ virus DNA and 5 μ g of the plasmid are mixed in a sterile well of a microtiter plate containing 50 μ l of serum-free Grace's medium (Life Technologies Inc., Gaithersburg, MD). Afterwards, 10 μ l Lipofectin plus 90 μ l
20 Grace's medium are added, mixed and incubated for 15 minutes at room temperature. Then the transfection mixture is added drop-wise to Sf9 insect cells (ATCC CRL 1711) seeded in a 35 mm tissue culture plate with 1 ml Grace's medium without serum. The plate is then incubated for 5 hours at 27° C. The transfection solution is then removed from the plate and 1 ml of Grace's insect medium supplemented with 10% fetal calf serum is added. Cultivation is then continued at 27° C
25 for four days.

After four days the supernatant is collected and a plaque assay is performed, as described by Summers and Smith, *supra*. An agarose gel with "Blue Gal" (Life Technologies Inc., Gaithersburg) is used to allow easy identification and isolation of gal-expressing clones, which produce blue-stained plaques. (A detailed description of a "plaque assay" of this type can also be
30 found in the user's guide for insect cell culture and baculovirology distributed by Life Technologies Inc., Gaithersburg, page 9-10.) After appropriate incubation, blue stained plaques are picked with the tip of a micropipettor (e.g., Eppendorf). The agar containing the recombinant viruses is then resuspended in a microcentrifuge tube containing 200 μ l of Grace's medium and the suspension containing the recombinant baculovirus is used to infect Sf9 cells seeded in 35 mm
35 dishes. Four days later the supernatants of these culture dishes are harvested and then they are stored at 4° C.

- To verify the expression of the polypeptide, Sf9 cells are grown in Grace's medium supplemented with 10% heat-inactivated FBS. The cells are infected with the recombinant baculovirus containing the polynucleotide at a multiplicity of infection ("MOI") of about 2. If radiolabeled proteins are desired, 6 hours later the medium is removed and is replaced with SF900
- 5 II medium minus methionine and cysteine (available from Life Technologies Inc., Rockville, MD). After 42 hours, 5 μ Ci of 35 S-methionine and 5 μ Ci 35 S-cysteine (available from Amersham) are added. The cells are further incubated for 16 hours and then are harvested by centrifugation. The proteins in the supernatant as well as the intracellular proteins are analyzed by SDS-PAGE followed by autoradiography (if radiolabeled).
- 10 Microsequencing of the amino acid sequence of the amino terminus of purified protein may be used to determine the amino terminal sequence of the produced protein.

Example 8: Expression of a Polypeptide in Mammalian Cells

- 15 The polypeptide of the present invention can be expressed in a mammalian cell. A typical mammalian expression vector contains a promoter element, which mediates the initiation of transcription of mRNA, a protein coding sequence, and signals required for the termination of transcription and polyadenylation of the transcript. Additional elements include enhancers, Kozak sequences and intervening sequences flanked by donor and acceptor sites for RNA splicing.
- 20 Highly efficient transcription is achieved with the early and late promoters from SV40, the long terminal repeats (LTRs) from Retroviruses, e.g., RSV, HTLV, HIV and the early promoter of the cytomegalovirus (CMV). However, cellular elements can also be used (e.g., the human actin promoter).

- Suitable expression vectors for use in practicing the present invention include, for
- 25 example, vectors such as pSVL and pMSG (Pharmacia, Uppsala, Sweden), pRSVcat (ATCC 37152), pSV2dhfr (ATCC 37146), pBC12MI (ATCC 67109), pCMVSPORT 2.0, and pCMVSPORT 3.0. Mammalian host cells that could be used include, human Hela, 293, H9 and Jurkat cells, mouse NIH3T3 and C127 cells, Cos 1, Cos 7 and CV1, quail QC1-3 cells, mouse L cells and Chinese hamster ovary (CHO) cells.

- 30 Alternatively, the polypeptide can be expressed in stable cell lines containing the polynucleotide integrated into a chromosome. The co-transfection with a selectable marker such as DHFR, gpt, neomycin, or hygromycin allows the identification and isolation of the transfected cells.

- The transfected gene can also be amplified to express large amounts of the encoded
- 35 protein. The DHFR (dihydrofolate reductase) marker is useful in developing cell lines that carry several hundred or even several thousand copies of the gene of interest. (See, e.g., Alt, F. W., et

al., J. Biol. Chem. 253:1357-1370 (1978); Hamlin, J. L. and Ma, C., Biochem. et Biophys. Acta, 1097:107-143 (1990); Page, M. J. and Sydenham, M. A., Biotechnology 9:64-68 (1991)). Another useful selection marker is the enzyme glutamine synthase (GS) (Murphy et al., Biochem J. 227:277-279 (1991); Bebbington et al., Bio/Technology 10:169-175 (1992). Using these markers, the mammalian cells are grown in selective medium and the cells with the highest resistance are selected. These cell lines contain the amplified gene(s) integrated into a chromosome. Chinese hamster ovary (CHO) and NSO cells are often used for the production of proteins.

Derivatives of the plasmid pSV2-dhfr (ATCC Accession No. 37146), the expression vectors pC4 (ATCC Accession No. 209646) and pC6 (ATCC Accession No. 209647) contain the strong promoter (LTR) of the Rous Sarcoma Virus (Cullen et al., Molecular and Cellular Biology, 438-447 (March, 1985)) plus a fragment of the CMV-enhancer (Boshart et al., Cell 41:521-530 (1985)). Multiple cloning sites, e.g., with the restriction enzyme cleavage sites BamHI, XbaI and Asp718, facilitate the cloning of the gene of interest. The vectors also contain the 3' intron, the polyadenylation and termination signal of the rat preproinsulin gene, and the mouse DHFR gene under control of the SV40 early promoter.

Specifically, the plasmid pC6, for example, is digested with appropriate restriction enzymes and then dephosphorylated using calf intestinal phosphates by procedures known in the art. The vector is then isolated from a 1% agarose gel.

A polynucleotide of the present invention is amplified according to the protocol outlined in Example 1. If a naturally occurring signal sequence is used to produce the polypeptide of the present invention, the vector does not need a second signal peptide. Alternatively, if a naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., International Publication No. WO 96/34891.)

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("GeneClean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The amplified fragment is then digested with the same restriction enzyme and purified on a 1% agarose gel. The isolated fragment and the dephosphorylated vector are then ligated with T4 DNA ligase. *E. coli* HB101 or XL-1 Blue cells are then transformed and bacteria are identified that contain the fragment inserted into plasmid pC6 using, for instance, restriction enzyme analysis.

Chinese hamster ovary cells lacking an active DHFR gene is used for transfection. Five μ g of the expression plasmid pC6 or pC4 is cotransfected with 0.5 μ g of the plasmid pSVneo using lipofectin (Felgner et al., *supra*). The plasmid pSV2-neo contains a dominant selectable marker, the *neo* gene from Tn5 encoding an enzyme that confers resistance to a group of antibiotics including G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are trypsinized and seeded in hybridoma cloning plates

(Greiner, Germany) in alpha minus MEM supplemented with 10, 25, or 50 ng/ml of methotrexate plus 1 mg/ml G418. After about 10-14 days single clones are trypsinized and then seeded in 6-well petri dishes or 10 ml flasks using different concentrations of methotrexate (50 nM, 100 nM, 200 nM, 400 nM, 800 nM). Clones growing at the highest concentrations of methotrexate are then transferred to new 6-well plates containing even higher concentrations of methotrexate (1 μ M, 2 μ M, 5 μ M, 10 mM, 20 mM). The same procedure is repeated until clones are obtained which grow at a concentration of 100 - 200 μ M. Expression of the desired gene product is analyzed, for instance, by SDS-PAGE and Western blot or by reversed phase HPLC analysis.

10

Example 9: Protein Fusions

The polypeptides of the present invention are preferably fused to other proteins. These fusion proteins can be used for a variety of applications. For example, fusion of the present polypeptides to His-tag, HA-tag, protein A, IgG domains, and maltose binding protein facilitates purification. (See Example 5; see also EP A 394,827; Traunecker, et al., Nature 331:84-86 (1988)). Similarly, fusion to IgG-1, IgG-3, and albumin increases the half-life time *in vivo*. Nuclear localization signals fused to the polypeptides of the present invention can target the protein to a specific subcellular localization, while covalent heterodimer or homodimers can increase or decrease the activity of a fusion protein. Fusion proteins can also create chimeric molecules having more than one function. Finally, fusion proteins can increase solubility and/or stability of the fused protein compared to the non-fused protein. All of the types of fusion proteins described above can be made by modifying the following protocol, which outlines the fusion of a polypeptide to an IgG molecule, or the protocol described in Example 5.

Briefly, the human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5' and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an expression vector, preferably a mammalian expression vector.

For example, if pC4 (ATCC Accession No. 209646) is used, the human Fc portion can be ligated into the BamHI cloning site. Note that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the vector, and a polynucleotide of the present invention, isolated by the PCR protocol described in Example 1, is ligated into this BamHI site. Note that the polynucleotide is cloned without a stop codon, otherwise a fusion protein will not be produced.

If the naturally occurring signal sequence is used to produce the polypeptide of the present invention, pC4 does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., International Publication No. WO 96/34891.)

Human IgG Fc region:

GGGATCCGGAGCCCAAATCTTCTGACAAACTCACACATGCCCACCGTGCCCA
 GCACCTGAATTCGAGGGTGCACCGTCAGTCTTCCTCTTCCCCCAAAACCCAAGGACA
 5 CCCTCATGATCTCCCGGACTCCTGAGGTCACATGCGTGGTGGTGGACGTAAGCCACGA
 AGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAA
 GACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCTCAC
 CGTCTTGCAACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAA
 AGCCCTCCCAACCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGA
 10 ACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAG
 CCTGACCTGCCTGGTCAAAGGCTTCTATCCAAGCGACATCGCCGTGGAGTGGGAGAG
 CAATGGGCAGCCGGAGAACAACACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGG
 CTCCTTCTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAA
 CGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGC
 15 CTCTCCCTGTCTCCGGGTAAATGAGTGCGACGGCCGCGACTCTAGAGGAT (SEQ ID
 NO: 1)

Example 10: Production of an Antibody from a Polypeptide

20 a) Hybridoma Technology

The antibodies of the present invention can be prepared by a variety of methods. (See, Current Protocols, Chapter 2.) As one example of such methods, cells expressing a polypeptide of the present invention are administered to an animal to induce the production of sera containing polyclonal antibodies. In a preferred method, a preparation of a polypeptide of the present
 25 invention is prepared and purified to render it substantially free of natural contaminants. Such a preparation is then introduced into an animal in order to produce polyclonal antisera of greater specific activity.

Monoclonal antibodies specific for a polypeptide of the present invention are prepared using hybridoma technology (Kohler et al., Nature 256:495 (1975); Kohler et al., Eur. J. Immunol. 6:511 (1976); Kohler et al., Eur. J. Immunol. 6:292 (1976); Hammerling et al., in: Monoclonal Antibodies and T-Cell Hybridomas, Elsevier, N.Y., pp. 563-681 (1981)). In general, an animal (preferably a mouse) is immunized with a polypeptide of the present invention or, more preferably, with a secreted polypeptide-expressing cell. Such polypeptide-expressing cells are cultured in any
 30 suitable tissue culture medium, preferably in Earle's modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at about 56°C), and supplemented with about 10 g/l of nonessential amino acids, about 1,000 U/ml of penicillin, and about 100 µg/ml of streptomycin.

The splenocytes of such mice are extracted and fused with a suitable myeloma cell line. Any suitable myeloma cell line may be employed in accordance with the present invention; however, it is preferable to employ the parent myeloma cell line (SP2O), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as described by Wands et al. (Gastroenterology 80:225-232 (1981)). The hybridoma cells obtained through such a selection are then assayed to identify clones which secrete antibodies capable of binding the polypeptide of the present invention .

Alternatively, additional antibodies capable of binding to a polypeptide of the present invention can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens, and therefore, it is possible to obtain an antibody which binds to a second antibody. In accordance with this method, protein specific antibodies are used to immunize an animal, preferably a mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the polypeptide-specific antibody can be blocked by said polypeptide. Such antibodies comprise anti-idiotypic antibodies to the polypeptide-specific antibody and are used to immunize an animal to induce formation of further polypeptide-specific antibodies.

For *in vivo* use of antibodies in humans, an antibody is "humanized". Such antibodies can be produced using genetic constructs derived from hybridoma cells producing the monoclonal antibodies described above. Methods for producing chimeric and humanized antibodies are known in the art and are discussed herein. (See, for review, Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496; Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., International Publication.No. WO 8702671; Boulianne et al., Nature 312:643 (1984); Neuberger et al., Nature 314:268 (1985)).

b) Isolation Of Antibody Fragments Directed Against a Polypeptide of the Present Invention From A Library Of scFvs

Naturally occurring V-genes isolated from human PBLs are constructed into a library of antibody fragments which contain reactivities against a polypeptide of the present invention to which the donor may or may not have been exposed (see e.g., U.S. Patent 5,885,793 incorporated herein by reference in its entirety).

Rescue of the Library. A library of scFvs is constructed from the RNA of human PBLs as described in International Publication No. WO 92/01047. To rescue phage displaying antibody fragments, approximately 10^9 *E. coli* harboring the phagemid are used to inoculate 50 ml of 2xTY containing 1% glucose and 100 μ g/ml of ampicillin (2xTY-AMP-GLU) and grown to an O.D. of 0.8 with shaking. Five ml of this culture is used to inoculate 50 ml of 2xTY-AMP-GLU, 2 x 10^8

TU of delta gene 3 helper (M13 delta gene III, see International Publication No. WO 92/01047) are added and the culture incubated at 37°C for 45 minutes without shaking and then at 37°C for 45 minutes with shaking. The culture is centrifuged at 4000 r.p.m. for 10 min. and the pellet resuspended in 2 liters of 2xTY containing 100 µg/ml ampicillin and 50 ug/ml kanamycin and
5 grown overnight. Phage are prepared as described in International Publication No. WO 92/01047.

M13 delta gene III is prepared as follows: M13 delta gene III helper phage does not encode gene III protein, hence the phage(mid) displaying antibody fragments have a greater avidity of binding to antigen. Infectious M13 delta gene III particles are made by growing the helper phage in cells harboring a pUC19 derivative supplying the wild type gene III protein during
10 phage morphogenesis. The culture is incubated for 1 hour at 37° C without shaking and then for a further hour at 37°C with shaking. Cells are spun down (IEC-Centra 8,400 r.p.m. for 10 min), resuspended in 300 ml 2xTY broth containing 100 µg ampicillin/ml and 25 µg kanamycin/ml (2xTY-AMP-KAN) and grown overnight, shaking at 37°C. Phage particles are purified and concentrated from the culture medium by two PEG-precipitations (Sambrook et al., 1990),
15 resuspended in 2 ml PBS and passed through a 0.45 µm filter (Minisart NML; Sartorius) to give a final concentration of approximately 10^{13} transducing units/ml (ampicillin-resistant clones).

Panning of the Library. Immuntubes (Nunc) are coated overnight in PBS with 4 ml of either 100 µg/ml or 10 µg/ml of a polypeptide of the present invention. Tubes are blocked with 2% Marvel-PBS for 2 hours at 37°C and then washed 3 times in PBS. Approximately 10^{13} TU of
20 phage is applied to the tube and incubated for 30 minutes at room temperature tumbling on an over and under turntable and then left to stand for another 1.5 hours. Tubes are washed 10 times with PBS 0.1% Tween-20 and 10 times with PBS. Phage are eluted by adding 1 ml of 100 mM triethylamine and rotating 15 minutes on an under and over turntable after which the solution is immediately neutralized with 0.5 ml of 1.0M Tris-HCl, pH 7.4. Phage are then used to infect 10
25 ml of mid-log E. coli TG1 by incubating eluted phage with bacteria for 30 minutes at 37°C. The E. coli are then plated on TYE plates containing 1% glucose and 100 µg/ml ampicillin. The resulting bacterial library is then rescued with delta gene 3 helper phage as described above to prepare phage for a subsequent round of selection. This process is then repeated for a total of 4 rounds of affinity purification with tube-washing increased to 20 times with PBS, 0.1% Tween-20
30 and 20 times with PBS for rounds 3 and 4.

Characterization of Binders. Eluted phage from the 3rd and 4th rounds of selection are used to infect E. coli HB 2151 and soluble scFv is produced (Marks, et al., 1991) from single colonies for assay. ELISAs are performed with microtitre plates coated with either 10 pg/ml of the polypeptide of the present invention in 50 mM bicarbonate pH 9.6. Clones positive in ELISA are
35 further characterized by PCR fingerprinting (see, e.g., International Publication No. WO 92/01047) and then by sequencing. These ELISA positive clones may also be further characterized by techniques known in the art, such as, for example, epitope mapping, binding

affinity, receptor signal transduction, ability to block or competitively inhibit antibody/antigen binding, and competitive agonistic or antagonistic activity.

Example 11: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide

5

RNA isolated from entire families or individual patients presenting with cancer or a hyperproliferative disease or disorder is isolated. cDNA is then generated from these RNA samples using protocols known in the art. (See, Sambrook.) The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO:X; and/or the nucleotide sequence of the cDNA contained in ATCC Deposit No:Z. Suggested PCR conditions consist of 35 cycles at 95 degrees C for 30 seconds; 60-120 seconds at 52-58 degrees C; and 60-120 seconds at 70 degrees C, using buffer solutions described in Sidransky et al., Science 252:706 (1991).

15 PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase (Epicentre Technologies). The intron-exon boundaries of selected exons is also determined and genomic PCR products analyzed to confirm the results. PCR products harboring suspected mutations are then cloned and sequenced to validate the results of the direct sequencing.

20 PCR products are cloned into T-tailed vectors as described in Holton et al., Nucleic Acids Research, 19:1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

Genomic rearrangements are also observed as a method of determining alterations in a gene corresponding to a polynucleotide. Genomic clones isolated according to Example 2 are nick-translated with digoxigenin deoxy-uridine 5'-triphosphate (Boehringer Mannheim), and FISH performed as described in Johnson et al., Methods Cell Biol. 35:73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium iodide, producing a combination of C- and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and variable excitation wavelength filters. (Johnson et al., Genet. Anal. Tech. Appl., 8:75 (1991)). Image collection, analysis and chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an associated disease.

Example 12: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample

5 A polypeptide of the present invention can be detected in a biological sample, and if an increased or decreased level of the polypeptide is detected, this polypeptide is a marker for a particular phenotype. Methods of detection are numerous, and thus, it is understood that one skilled in the art can modify the following assay to fit their particular needs.

10 For example, antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described in Example 10. The wells are blocked so that non-specific binding of the polypeptide to the well is reduced.

15 The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbound polypeptide.

20 Next, 50 ul of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbound conjugate.

25 Add 75 ul of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution to each well and incubate 1 hour at room temperature. Measure the reaction by a microtiter plate reader. Prepare a standard curve, using serial dilutions of a control sample, and plot polypeptide concentration on the X-axis (log scale) and fluorescence or absorbance of the Y-axis (linear scale). Interpolate the concentration of the polypeptide in the sample using the standard curve.

Example 13: Formulation

30 The invention also provides methods of preventing, treating and/or ameliorating cancer or other hyperproliferative disorders by administration to a subject of an effective amount of a Therapeutic. By therapeutic is meant polynucleotides or polypeptides of the invention (including fragments and variants), agonists or antagonists thereof, and/or antibodies thereto, in combination with a pharmaceutically acceptable carrier type (e.g., a sterile carrier).

35 The Therapeutic will be formulated and dosed in a fashion consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the Therapeutic alone), the site of delivery, the method of administration,

the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of the Therapeutic administered parenterally per dose will be in the range of about 1 μ g/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given continuously, the Therapeutic is typically administered at a dose rate of about 1 μ g/kg/hour to about 50 μ g/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

Therapeutics can be administered orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), buccally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

Therapeutics of the invention are also suitably administered by sustained-release systems. Suitable examples of sustained-release Therapeutics are administered orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), buccally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

Therapeutics of the invention are also suitably administered by sustained-release systems. Suitable examples of sustained-release Therapeutics include suitable polymeric materials (such as, for example, semi-permeable polymer matrices in the form of shaped articles, e.g., films, or microcapsules), suitable hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, and sparingly soluble derivatives (such as, for example, a sparingly soluble salt).

Sustained-release matrices include polylactides (U.S. Pat. No. 3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman et al., Biopolymers 22:547-556 (1983)), poly (2-hydroxyethyl methacrylate) (Langer et al., J. Biomed. Mater. Res.

15:167-277 (1981), and Langer, Chem. Tech. 12:98-105 (1982)), ethylene vinyl acetate (Langer et al., Id.) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988).

In a preferred embodiment, polypeptide, polynucleotide, and antibody compositions of the invention are formulated in a biodegradable, polymeric drug delivery system, for example as
5 described in U.S. Patent Nos. 4,938,763; 5,278,201; 5,278,202; 5,324,519; 5,340,849; and 5,487,897 and in International Publication Numbers WO01/35929, WO00/24374, and WO00/06117 which are hereby incorporated by reference in their entirety. In specific preferred embodiments the polypeptide, polynucleotide, and antibody compositions of the invention are formulated using the ATRIGEL® Biodegradable System of Atrix Laboratories, Inc. (Fort Collins,
10 Colorado).

Examples of biodegradable polymers which can be used in the formulation of polypeptide, polynucleotide, and antibody compositions, include but are not limited to, polylactides, polyglycolides, polycaprolactones, polyanhydrides, polyamides, polyurethanes, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates, polyorthocarbonates,
15 polyphosphazenes, polyhydroxybutyrates, polyhydroxyvalerates, polyalkylene oxalates, polyalkylene succinates, poly(malic acid), poly(amino acids), poly(methyl vinyl ether), poly(maleic anhydride), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, chitin, chitosan, and copolymers, terpolymers, or combinations or mixtures of the above materials. The preferred polymers are those that have a lower degree of crystallization and are more hydrophobic.
20 These polymers and copolymers are more soluble in the biocompatible solvents than the highly crystalline polymers such as polyglycolide and chitin which also have a high degree of hydrogen-bonding. Preferred materials with the desired solubility parameters are the polylactides, polycaprolactones, and copolymers of these with glycolide in which there are more amorphous regions to enhance solubility. In specific preferred embodiments, the biodegradable polymers
25 which can be used in the formulation of polypeptide, polynucleotide, and antibody compositions are poly(lactide-co-glycolides). Polymer properties such as molecular weight, hydrophobicity, and lactide/glycolide ratio may be modified to obtain the desired polypeptide, polynucleotide, or antibody release profile (See, e.g., Ravivarapu et al., Journal of Pharmaceutical Sciences 89:732-741 (2000), which is hereby incorporated by reference in its entirety).

30 It is also preferred that the solvent for the biodegradable polymer be non-toxic, water miscible, and otherwise biocompatible. Examples of such solvents include, but are not limited to, N-methyl-2-pyrrolidone, 2-pyrrolidone, C2 to C6 alkanols, C1 to C15 alcohols, diols, triols, and tetraols such as ethanol, glycerine propylene glycol, butanol; C3 to C15 alkyl ketones such as acetone, diethyl ketone and methyl ethyl ketone; C3 to C15 esters such as methyl acetate, ethyl acetate, ethyl lactate; alkyl ketones such as methyl ethyl ketone, C1 to C15 amides such as dimethylformamide, dimethylacetamide and caprolactam; C3 to C20 ethers such as tetrahydrofuran, or solketal; tweens, triacetin, propylene carbonate, decylmethylsulfoxide,
35

dimethyl sulfoxide, oleic acid, 1-dodecylazacycloheptan-2-one, Other preferred solvents are benzyl alcohol, benzyl benzoate, dipropylene glycol, tributyrin, ethyl oleate, glycerin, glycofural, isopropyl myristate, isopropyl palmitate, oleic acid, polyethylene glycol, propylene carbonate, and triethyl citrate. The most preferred solvents are N-methyl-2-pyrrolidone, 2-pyrrolidone, dimethyl sulfoxide, triacetin, and propylene carbonate because of the solvating ability and their compatibility.

Additionally, formulations comprising polypeptide, polynucleotide, and antibody compositions and a biodegradable polymer may also include release-rate modification agents and/or pore-forming agents. Examples of release-rate modification agents include, but are not limited to, fatty acids, triglycerides, other like hydrophobic compounds, organic solvents, plasticizing compounds and hydrophilic compounds. Suitable release rate modification agents include, for example, esters of mono-, di-, and tricarboxylic acids, such as 2-ethoxyethyl acetate, methyl acetate, ethyl acetate, diethyl phthalate, dimethyl phthalate, dibutyl phthalate, dimethyl adipate, dimethyl succinate, dimethyl oxalate, dimethyl citrate, triethyl citrate, acetyl tributyl citrate, acetyl triethyl citrate, glycerol triacetate, di(n-butyl) sebacate, and the like; polyhydroxy alcohols, such as propylene glycol, polyethylene glycol, glycerin, sorbitol, and the like; fatty acids; triesters of glycerol, such as triglycerides, epoxidized soybean oil, and other epoxidized vegetable oils; sterols, such as cholesterol; alcohols, such as C.sub.6 -C.sub.12 alkanols, 2-ethoxyethanol. The release rate modification agent may be used singly or in combination with other such agents. Suitable combinations of release rate modification agents include, but are not limited to, glycerin/propylene glycol, sorbitol/glycerine, ethylene oxide/propylene oxide, butylene glycol/adipic acid, and the like. Preferred release rate modification agents include, but are not limited to, dimethyl citrate, triethyl citrate, ethyl heptanoate, glycerin, and hexanediol. Suitable pore-forming agents that may be used in the polymer composition include, but are not limited to, sugars such as sucrose and dextrose, salts such as sodium chloride and sodium carbonate, polymers such as hydroxylpropylcellulose, carboxymethylcellulose, polyethylene glycol, and polyvinylpyrrolidone. Solid crystals that will provide a defined pore size, such as salt or sugar, are preferred.

In specific preferred embodiments the polypeptide, polynucleotide, and antibody compositions of the invention are formulated using the BEMA™ BioErodible Mucoadhesive System, MCA™ MucoCutaneous Absorption System, SMPT™ Solvent MicroParticle System, or BCPT™ BioCompatible Polymer System of Atrix Laboratories, Inc. (Fort Collins, Colorado).

Sustained-release Therapeutics also include liposomally entrapped Therapeutics of the invention (see generally, Langer, *Science* 249:1527-1533 (1990); Treat et al., in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 317-327 and 353-365 (1989)). Liposomes containing the Therapeutic are prepared by methods known per se: DE 3,218,121; Epstein et al., *Proc. Natl. Acad. Sci. (USA)* 82:3688-3692 (1985);

Hwang et al., Proc. Natl. Acad. Sci.(USA) 77:4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal Therapeutic.

In yet an additional embodiment, the Therapeutics of the invention are delivered by way of a pump (*see* Langer, *supra*; Sefton, CRC Crit. Ref. Biomed. Eng. 14:201 (1987); Buchwald et al., Surgery 88:507 (1980); Saudek et al., N. Engl. J. Med. 321:574 (1989)).

Other controlled release systems are discussed in the review by Langer (*Science* 249:1527-1533 (1990)).

For parenteral administration, in one embodiment, the Therapeutic is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation. For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to the Therapeutic.

Generally, the formulations are prepared by contacting the Therapeutic uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is shaped into the desired formulation. Preferably the carrier is a parenteral carrier, more preferably a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.

The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e.g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The Therapeutic is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

Any pharmaceutical used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutics generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

5 Therapeutics ordinarily will be stored in unit or multi-dose containers, for example, sealed ampoules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1% (w/v) aqueous Therapeutic solution, and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized Therapeutic using bacteriostatic Water-for-Injection.

10 The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the Therapeutics of the invention. Associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition,
15 the Therapeutics may be employed in conjunction with other therapeutic compounds.

 The Therapeutics of the invention may be administered alone or in combination with adjuvants. Adjuvants that may be administered with the Therapeutics of the invention include, but are not limited to, alum, alum plus deoxycholate (ImmunoAg), MTP-PE (Biocine Corp.), QS21 (Genentech, Inc.), BCG (e.g., THERACYS®), MPL and nonviable preparations of
20 *Corynebacterium parvum*. In a specific embodiment, Therapeutics of the invention are administered in combination with alum. In another specific embodiment, Therapeutics of the invention are administered in combination with QS-21. Further adjuvants that may be administered with the Therapeutics of the invention include, but are not limited to, Monophosphoryl lipid immunomodulator, AdjuVax 100a, QS-21, QS-18, CRL1005, Aluminum
25 salts, MF-59, and Virosomal adjuvant technology. Vaccines that may be administered with the Therapeutics of the invention include, but are not limited to, vaccines directed toward protection against MMR (measles, mumps, rubella), polio, varicella, tetanus/diphtheria, hepatitis A, hepatitis B, haemophilus influenzae B, whooping cough, pneumonia, influenza, Lyme's Disease, rotavirus, cholera, yellow fever, Japanese encephalitis, poliomyelitis, rabies, typhoid fever, and pertussis.
30 Combinations may be administered either concomitantly, e.g., as an admixture, separately but simultaneously or concurrently; or sequentially. This includes presentations in which the combined agents are administered together as a therapeutic mixture, and also procedures in which the combined agents are administered separately but simultaneously, e.g., as through separate intravenous lines into the same individual. Administration "in combination" further includes the
35 separate administration of one of the compounds or agents given first, followed by the second.

 The Therapeutics of the invention may be administered alone or in combination with other therapeutic agents. Therapeutic agents that may be administered in combination with the

Therapeutics of the invention, include but not limited to, chemotherapeutic agents, antibiotics, steroidal and non-steroidal anti-inflammatories, conventional immunotherapeutic agents, and/or therapeutic treatments described below. Combinations may be administered either concomitantly, e.g., as an admixture, separately but simultaneously or concurrently; or sequentially. This includes
5 presentations in which the combined agents are administered together as a therapeutic mixture, and also procedures in which the combined agents are administered separately but simultaneously, e.g., as through separate intravenous lines into the same individual. Administration "in combination" further includes the separate administration of one of the compounds or agents given first, followed by the second.

10 In one embodiment, the Therapeutics of the invention are administered in combination with an anticoagulant. Anticoagulants that may be administered with the compositions of the invention include, but are not limited to, heparin, low molecular weight heparin, warfarin sodium (e.g., COUMADIN®), dicumarol, 4-hydroxycoumarin, anisindione (e.g., MIRADON™), acenocoumarol (e.g., nicoumalone, SINTHROME™), indan-1,3-dione, phenprocoumon (e.g.,
15 MARCUMAR™), ethyl biscoumacetate (e.g., TROMEXAN™), and aspirin. In a specific embodiment, compositions of the invention are administered in combination with heparin and/or warfarin. In another specific embodiment, compositions of the invention are administered in combination with warfarin. In another specific embodiment, compositions of the invention are administered in combination with warfarin and aspirin. In another specific embodiment,
20 compositions of the invention are administered in combination with heparin. In another specific embodiment, compositions of the invention are administered in combination with heparin and aspirin.

In another embodiment, the Therapeutics of the invention are administered in combination with thrombolytic drugs. Thrombolytic drugs that may be administered with the compositions of
25 the invention include, but are not limited to, plasminogen, lys-plasminogen, alpha2-antiplasmin, streptokinase (e.g., KABIKINASE™), antirespace (e.g., EMINASE™), tissue plasminogen activator (t-PA, altevase, ACTIVASE™), urokinase (e.g., ABBOKINASE™), sauruplase, (Prourokinase, single chain urokinase), and aminocaproic acid (e.g., AMICAR™). In a specific embodiment, compositions of the invention are administered in combination with tissue
30 plasminogen activator and aspirin.

In another embodiment, the Therapeutics of the invention are administered in combination with antiplatelet drugs. Antiplatelet drugs that may be administered with the compositions of the invention include, but are not limited to, aspirin, dipyridamole (e.g., PERSANTINE™), and ticlopidine (e.g., TICLID™).

35 In specific embodiments, the use of anti-coagulants, thrombolytic and/or antiplatelet drugs in combination with Therapeutics of the invention is contemplated for the detection, prevention, diagnosis, prognostication, treatment, and/or amelioration of thrombosis, arterial thrombosis,

venous thrombosis, thromboembolism, pulmonary embolism, atherosclerosis, myocardial infarction, transient ischemic attack, unstable angina. In specific embodiments, the use of anticoagulants, thrombolytic drugs and/or antiplatelet drugs in combination with Therapeutics of the invention is contemplated for the prevention of occlusion of saphenous grafts, for reducing the risk of periprocedural thrombosis as might accompany angioplasty procedures, for reducing the risk of stroke in patients with atrial fibrillation including nonrheumatic atrial fibrillation, for reducing the risk of embolism associated with mechanical heart valves and or mitral valves disease. Other uses for the therapeutics of the invention, alone or in combination with antiplatelet, anticoagulant, and/or thrombolytic drugs, include, but are not limited to, the prevention of occlusions in extracorporeal devices (e.g., intravascular canulas, vascular access shunts in hemodialysis patients, hemodialysis machines, and cardiopulmonary bypass machines).

In certain embodiments, Therapeutics of the invention are administered in combination with antiretroviral agents, nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and/or protease inhibitors (PIs). NRTIs that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, RETROVIR™ (zidovudine/AZT), VIDEX™ (didanosine/ddI), HIVID™ (zalcitabine/ddC), ZERIT™ (stavudine/d4T), EPIVIR™ (lamivudine/3TC), and COMBIVIR™ (zidovudine/lamivudine). NNRTIs that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, VIRAMUNE™ (nevirapine), RESCRIPTOR™ (delavirdine), and SUSTIVA™ (efavirenz). Protease inhibitors that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, CRIXIVAN™ (indinavir), NORVIR™ (ritonavir), INVIRASE™ (saquinavir), and VIRACEPT™ (nelfinavir). In a specific embodiment, antiretroviral agents, nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and/or protease inhibitors may be used in any combination with Therapeutics of the invention to treat AIDS and/or to prevent or treat HIV infection.

Additional NRTIs include LODENOSINE™ (F-ddA; an acid-stable adenosine NRTI; Triangle/Abbott; COVIRACIL™ (emtricitabine/FTC; structurally related to lamivudine (3TC) but with 3- to 10-fold greater activity *in vitro*; Triangle/Abbott); dOTC (BCH-10652, also structurally related to lamivudine but retains activity against a substantial proportion of lamivudine-resistant isolates; Biochem Pharma); Adefovir (refused approval for anti-HIV therapy by FDA; Gilead Sciences); PREVEON® (Adefovir Dipivoxil, the active prodrug of adefovir; its active form is PMEA-pp); TENOFOVIR™ (bis-POC PMPA, a PMPA prodrug; Gilead); DAPD/DXG (active metabolite of DAPD; Triangle/Abbott); D-D4FC (related to 3TC, with activity against AZT/3TC-resistant virus); GW420867X (Glaxo Wellcome); ZIAGEN™ (abacavir/159U89; Glaxo Wellcome

Inc.); CS-87 (3'-azido-2',3'-dideoxyuridine; WO 99/66936); and S-acyl-2-thioethyl (SATE)-bearing prodrug forms of β -L-FD4C and β -L-FddC (WO 98/17281).

Additional NNRTIs include COACTINON™ (Emivirine/MKC-442, potent NNRTI of the HEPT class; Triangle/Abbott); CAPRAVIRINE™ (AG-1549/S-1153, a next generation NNRTI with activity against viruses containing the K103N mutation; Agouron); PNU-142721 (has 20- to 50-fold greater activity than its predecessor delavirdine and is active against K103N mutants; Pharmacia & Upjohn); DPC-961 and DPC-963 (second-generation derivatives of efavirenz, designed to be active against viruses with the K103N mutation; DuPont); GW-420867X (has 25-fold greater activity than HBY097 and is active against K103N mutants; Glaxo Wellcome); CALANOLIDE A (naturally occurring agent from the latex tree; active against viruses containing either or both the Y181C and K103N mutations); and Propolis (WO 99/49830).

Additional protease inhibitors include LOPINAVIR™ (ABT378/r; Abbott Laboratories); BMS-232632 (an azapeptide; Bristol-Myers Squibb); TIPRANAVIR™ (PNU-140690, a non-peptidic dihydropyrene; Pharmacia & Upjohn); PD-178390 (a nonpeptidic dihydropyrene; Parke-Davis); BMS 232632 (an azapeptide; Bristol-Myers Squibb); L-756,423 (an indinavir analog; Merck); DMP-450 (a cyclic urea compound; Avid & DuPont); AG-1776 (a peptidomimetic with *in vitro* activity against protease inhibitor-resistant viruses; Agouron); VX-175/GW-433908 (phosphate prodrug of amprenavir; Vertex & Glaxo Wellcome); CGP61755 (Ciba); and AGENERASE™ (amprenavir; Glaxo Wellcome Inc.).

Additional antiretroviral agents include fusion inhibitors/gp41 binders. Fusion inhibitors/gp41 binders include T-20 (a peptide from residues 643-678 of the HIV gp41 transmembrane protein ectodomain which binds to gp41 in its resting state and prevents transformation to the fusogenic state; Trimeris) and T-1249 (a second-generation fusion inhibitor; Trimeris).

Additional antiretroviral agents include fusion inhibitors/chemokine receptor antagonists. Fusion inhibitors/chemokine receptor antagonists include CXCR4 antagonists such as AMD 3100 (a bicyclam), SDF-1 and its analogs, and ALX40-4C (a cationic peptide), T22 (an 18 amino acid peptide; Trimeris) and the T22 analogs T134 and T140; CCR5 antagonists such as RANTES (9-68), AOP-RANTES, NNY-RANTES, and TAK-779; and CCR5/CXCR4 antagonists such as NSC 651016 (a distamycin analog). Also included are CCR2B, CCR3, and CCR6 antagonists. Chemokine receptor agonists such as RANTES, SDF-1, MIP-1 α , MIP-1 β , etc., may also inhibit fusion.

Additional antiretroviral agents include integrase inhibitors. Integrase inhibitors include dicaffeoylquinic (DFQA) acids; L-chicoric acid (a dicaffeoyltartaric (DCTA) acid); quinalizarin (QLC) and related anthraquinones; ZINTEVIR™ (AR 177, an oligonucleotide that probably acts at

cell surface rather than being a true integrase inhibitor; Arondex); and naphthols such as those disclosed in WO 98/50347.

Additional antiretroviral agents include hydroxyurea-like compounds such as BCX-34 (a purine nucleoside phosphorylase inhibitor; Biocryst); ribonucleotide reductase inhibitors such as
 5 DIDOX™ (Molecules for Health); inosine monophosphate dehydrogenase (IMPDH) inhibitors such as VX-497 (Vertex); and mycopholic acids such as CellCept (mycophenolate mofetil; Roche).

Additional antiretroviral agents include inhibitors of viral integrase, inhibitors of viral genome nuclear translocation such as arylene bis(methylketone) compounds; inhibitors of HIV
 10 entry such as AOP-RANTES, NNY-RANTES, RANTES-IgG fusion protein, soluble complexes of RANTES and glycosaminoglycans (GAG), and AMD-3100; nucleocapsid zinc finger inhibitors such as dithiane compounds; targets of HIV Tat and Rev; and pharmacoenhancers such as ABT-378.

Other antiretroviral therapies and adjunct therapies include cytokines and lymphokines
 15 such as MIP-1 α , MIP-1 β , SDF-1 α , IL-2, PROLEUKIN™ (aldesleukin/L2-7001; Chiron), IL-4, IL-10, IL-12, and IL-13; interferons such as IFN- α 2a; antagonists of TNFs, NF κ B, GM-CSF, M-CSF, and IL-10; agents that modulate immune activation such as cyclosporin and prednisone; vaccines such as Remune™ (HIV Immunogen), APL 400-003 (Apollon), recombinant gp120 and fragments, bivalent (B/E) recombinant envelope glycoprotein, rgp120CM235, MN rgp120, SF-2
 20 rgp120, gp120/soluble CD4 complex, Delta JR-FL protein, branched synthetic peptide derived from discontinuous gp120 C3/C4 domain, fusion-competent immunogens, and Gag, Pol, Nef, and Tat vaccines; gene-based therapies such as genetic suppressor elements (GSEs; WO 98/54366), and intrakines (genetically modified CC chemokines targetted to the ER to block surface expression of newly synthesized CCR5 (Yang *et al.*, *PNAS* 94:11567-72 (1997); Chen *et al.*, *Nat.*
 25 *Med.* 3:1110-16 (1997)); antibodies such as the anti-CXCR4 antibody 12G5, the anti-CCR5 antibodies 2D7, 5C7, PA8, PA9, PA10, PA11, PA12, and PA14, the anti-CD4 antibodies Q4120 and RPA-T4, the anti-CCR3 antibody 7B11, the anti-gp120 antibodies 17b, 48d, 447-52D, 257-D, 268-D and 50.1, anti-Tat antibodies, anti-TNF- α antibodies, and monoclonal antibody 33A; aryl hydrocarbon (AH) receptor agonists and antagonists such as TCDD, 3,3',4,4',5-
 30 pentachlorobiphenyl, 3,3',4,4'-tetrachlorobiphenyl, and α -naphthoflavone (WO 98/30213); and antioxidants such as γ -L-glutamyl-L-cysteine ethyl ester (γ -GCE; WO 99/56764).

In a further embodiment, the Therapeutics of the invention are administered in combination with an antiviral agent. Antiviral agents that may be administered with the Therapeutics of the invention include, but are not limited to, acyclovir, ribavirin, amantadine, and
 35 remantidine.

In other embodiments, Therapeutics of the invention may be administered in combination with anti-opportunistic infection agents. Anti-opportunistic agents that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, TRIMETHOPRIM-SULFAMETHOXAZOLE™, DAPSONE™, PENTAMIDINE™, ATOVAQUONE™, ISONIAZID™, RIFAMPIN™, PYRAZINAMIDE™, ETHAMBUTOL™, RIFABUTIN™, CLARITHROMYCIN™, AZITHROMYCIN™, GANCICLOVIR™, FOSCARNET™, CIDOFOVIR™, FLUCONAZOLE™, ITRACONAZOLE™, KETOCONAZOLE™, ACYCLOVIR™, FAMCICOLVIR™, PYRIMETHAMINE™, LEUCOVORIN™, NEUPOGEN™ (filgrastim/G-CSF), and LEUKINE™ (sargramostim/GM-CSF). In a specific embodiment, Therapeutics of the invention are used in any combination with TRIMETHOPRIM-SULFAMETHOXAZOLE™, DAPSONE™, PENTAMIDINE™, and/or ATOVAQUONE™ to prophylactically treat or prevent an opportunistic *Pneumocystis carinii* pneumonia infection. In another specific embodiment, Therapeutics of the invention are used in any combination with ISONIAZID™, RIFAMPIN™, PYRAZINAMIDE™, and/or ETHAMBUTOL™ to prophylactically treat or prevent an opportunistic *Mycobacterium avium* complex infection. In another specific embodiment, Therapeutics of the invention are used in any combination with RIFABUTIN™, CLARITHROMYCIN™, and/or AZITHROMYCIN™ to prophylactically treat or prevent an opportunistic *Mycobacterium tuberculosis* infection. In another specific embodiment, Therapeutics of the invention are used in any combination with GANCICLOVIR™, FOSCARNET™, and/or CIDOFOVIR™ to prophylactically treat or prevent an opportunistic cytomegalovirus infection. In another specific embodiment, Therapeutics of the invention are used in any combination with FLUCONAZOLE™, ITRACONAZOLE™, and/or KETOCONAZOLE™ to prophylactically treat or prevent an opportunistic fungal infection. In another specific embodiment, Therapeutics of the invention are used in any combination with ACYCLOVIR™ and/or FAMCICOLVIR™ to prophylactically treat or prevent an opportunistic herpes simplex virus type I and/or type II infection. In another specific embodiment, Therapeutics of the invention are used in any combination with PYRIMETHAMINE™ and/or LEUCOVORIN™ to prophylactically treat or prevent an opportunistic *Toxoplasma gondii* infection. In another specific embodiment, Therapeutics of the invention are used in any combination with LEUCOVORIN™ and/or NEUPOGEN™ to prophylactically treat or prevent an opportunistic bacterial infection.

In a further embodiment, the Therapeutics of the invention are administered in combination with an antibiotic agent. Antibiotic agents that may be administered with the Therapeutics of the invention include, but are not limited to, amoxicillin, beta-lactamases, aminoglycosides, beta-lactam (glycopeptide), beta-lactamases, Clindamycin, chloramphenicol,

cephalosporins, ciprofloxacin, erythromycin, fluoroquinolones, macrolides, metronidazole, penicillins, quinolones, rapamycin, rifampin, streptomycin, sulfonamide, tetracyclines, trimethoprim, trimethoprim-sulfamethoxazole, and vancomycin.

In other embodiments, the Therapeutics of the invention are administered in combination with immunestimulants. Immunostimulants that may be administered in combination with the Therapeutics of the invention include, but are not limited to, levamisole (e.g., ERGAMISOL™), isoprinosine (e.g. INOSIPLEX™), interferons (e.g. interferon alpha), and interleukins (e.g., IL-2).

In other embodiments, Therapeutics of the invention are administered in combination with immunosuppressive agents. Immunosuppressive agents that may be administered in combination with the Therapeutics of the invention include, but are not limited to, steroids, cyclosporine, cyclosporine analogs, cyclophosphamide methylprednisone, prednisone, azathioprine, FK-506, 15-deoxyspergualin, and other immunosuppressive agents that act by suppressing the function of responding T cells. Other immunosuppressive agents that may be administered in combination with the Therapeutics of the invention include, but are not limited to, prednisolone, methotrexate, thalidomide, methoxsalen, rapamycin, leflunomide, mizoribine (BREDININ™), brequinar, deoxyspergualin, and azaspirane (SKF 105685), ORTHOCLONE OKT® 3 (muromonab-CD3), SANDIMMUNE™, NEORAL™, SANGDYA™ (cyclosporine), PROGRAF® (FK506, tacrolimus), CELLCEPT® (mycophenolate mofetil, of which the active metabolite is mycophenolic acid), IMURAN™ (azathioprine), glucocorticosteroids, adrenocortical steroids such as DELTASONE™ (prednisone) and HYDELTRASOL™ (prednisolone), FOLEXT™ and MEXATE™ (methotrxate), OXSORALEN-ULTRA™ (methoxsalen) and RAPAMUNE™ (sirolimus). In a specific embodiment, immunosuppressants may be used to prevent rejection of organ or bone marrow transplantation.

In an additional embodiment, Therapeutics of the invention are administered alone or in combination with one or more intravenous immune globulin preparations. Intravenous immune globulin preparations that may be administered with the Therapeutics of the invention include, but not limited to, GAMMAR™, IVEEGAM™, SANDOGLOBULIN™, GAMMAGARD S/D™, ATGAM™ (antithymocyte globulin), and GAMIMUNE™. In a specific embodiment, Therapeutics of the invention are administered in combination with intravenous immune globulin preparations in transplantation therapy (e.g., bone marrow transplant).

In certain embodiments, the Therapeutics of the invention are administered alone or in combination with an anti-inflammatory agent. Anti-inflammatory agents that may be administered with the Therapeutics of the invention include, but are not limited to, corticosteroids (e.g. betamethasone, budesonide, cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone, and triamcinolone), nonsteroidal anti-inflammatory drugs (e.g., diclofenac, diflunisal, etodolac, fenoprofen, floctafenine, flurbiprofen, ibuprofen, indomethacin,

ketoprofen, meclofenamate, mefenamic acid, meloxicam, nabumetone, naproxen, oxaprozin, phenylbutazone, piroxicam, sulindac, tenoxicam, tiaprofenic acid, and tolmetin.), as well as antihistamines, aminoarylcarboxylic acid derivatives, arylacetic acid derivatives, arylbutyric acid derivatives, arylcarboxylic acids, arylpropionic acid derivatives, pyrazoles, pyrazolones, salicylic acid derivatives, thiazinecarboxamides, e-acetamidocaproic acid, S-adenosylmethionine, 3-amino-4-hydroxybutyric acid, amixetrine, bendazac, benzydamine, bucolome, difenpiramide, ditazol, emorfazone, guaiazulene, nabumetone, nimesulide, orgotein, oxaceprol, paranyline, perisoxal, pifoxime, proquazone, proxazole, and tenidap.

In an additional embodiment, the compositions of the invention are administered alone or in combination with an anti-angiogenic agent. Anti-angiogenic agents that may be administered with the compositions of the invention include, but are not limited to, Angiostatin (Entremed, Rockville, MD), Troponin-1 (Boston Life Sciences, Boston, MA), anti-Invasive Factor, retinoic acid and derivatives thereof, paclitaxel (Taxol), Suramin, Tissue Inhibitor of Metalloproteinase-1, Tissue Inhibitor of Metalloproteinase-2, VEGI, Plasminogen Activator Inhibitor-1, Plasminogen Activator Inhibitor-2, and various forms of the lighter "d group" transition metals.

Lighter "d group" transition metals include, for example, vanadium, molybdenum, tungsten, titanium, niobium, and tantalum species. Such transition metal species may form transition metal complexes. Suitable complexes of the above-mentioned transition metal species include oxo transition metal complexes.

Representative examples of vanadium complexes include oxo vanadium complexes such as vanadate and vanadyl complexes. Suitable vanadate complexes include metavanadate and orthovanadate complexes such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates.

Representative examples of tungsten and molybdenum complexes also include oxo complexes. Suitable oxo tungsten complexes include tungstate and tungsten oxide complexes. Suitable tungstate complexes include ammonium tungstate, calcium tungstate, sodium tungstate dihydrate, and tungstic acid. Suitable tungsten oxides include tungsten (IV) oxide and tungsten (VI) oxide. Suitable oxo molybdenum complexes include molybdate, molybdenum oxide, and molybdenyl complexes. Suitable molybdate complexes include ammonium molybdate and its hydrates, sodium molybdate and its hydrates, and potassium molybdate and its hydrates. Suitable molybdenum oxides include molybdenum (VI) oxide, molybdenum (VI) oxide, and molybdic acid. Suitable molybdenyl complexes include, for example, molybdenyl acetylacetonate. Other suitable tungsten and molybdenum complexes include hydroxo derivatives derived from, for example, glycerol, tartaric acid, and sugars.

A wide variety of other anti-angiogenic factors may also be utilized within the context of the present invention. Representative examples include, but are not limited to, platelet factor 4; protamine sulphate; sulphated chitin derivatives (prepared from queen crab shells), (Murata et al., Cancer Res. 51:22-26, (1991)); Sulphated Polysaccharide Peptidoglycan Complex (SP- PG) (the
 5 function of this compound may be enhanced by the presence of steroids such as estrogen, and tamoxifen citrate); Staurosporine; modulators of matrix metabolism, including for example, proline analogs, cishydroxyproline, d,L-3,4-dehydroproline, Thiaproline, alpha,alpha-dipyridyl, aminopropionitrile fumarate; 4-propyl-5-(4-pyridinyl)-2(3H)-oxazolone; Methotrexate; Mitoxantrone; Heparin; Interferons; 2 Macroglobulin-serum; ChIMP-3 (Pavloff et al., J. Bio.
 10 Chem. 267:17321-17326, (1992)); Chymostatin (Tomkinson et al., Biochem J. 286:475-480, (1992)); Cyclodextrin Tetradecasulfate; Eponemycin; Camptothecin; Fumagillin (Ingber et al., Nature 348:555-557, (1990)); Gold Sodium Thiomalate ("GST"; Matsubara and Ziff, J. Clin. Invest. 79:1440-1446, (1987)); anticollagenase-serum; alpha2-antiplasmin (Holmes et al., J. Biol. Chem. 262(4):1659-1664, (1987)); Bisantrene (National Cancer Institute); Lobenzarit disodium
 15 (N-(2)-carboxyphenyl-4- chloroanthronilic acid disodium or "CCA"; (Takeuchi et al., Agents Actions 36:312-316, (1992)); and metalloproteinase inhibitors such as BB94.

Additional anti-angiogenic factors that may also be utilized within the context of the present invention include Thalidomide, (Celgene, Warren, NJ); Angiostatic steroid; AGM-1470 (H. Brem and J. Folkman *J Pediatr. Surg.* 28:445-51 (1993)); an integrin alpha v beta 3 antagonist
 20 (C. Storgard et al., *J Clin. Invest.* 103:47-54 (1999)); carboxynaminolmidazole; Carboxyamidotriazole (CAI) (National Cancer Institute, Bethesda, MD); Conbretastatin A-4 (CA4P) (OXiGENE, Boston, MA); Squalamine (Magainin Pharmaceuticals, Plymouth Meeting, PA); TNP-470, (Tap Pharmaceuticals, Deerfield, IL); ZD-0101 AstraZeneca (London, UK); APRA (CT2584); Benefin, Byrostatin-1 (SC339555); CGP-41251 (PKC 412); CM101;
 25 Dexrazoxane (ICRF187); DMXAA; Endostatin; Flavopridiol; Genestein; GTE; ImmTher; Iressa (ZD1839); Octreotide (Somatostatin); Panretin; Penacillamine; Photopoint; PI-88; Prinomastat (AG-3340) Purlitin; Suradista (FCE26644); Tamoxifen (Nolvadex); Tazarotene; Tetrathiomolybdate; Xeloda (Capecitabine); and 5-Fluorouracil.

Anti-angiogenic agents that may be administered in combination with the compounds of the
 30 invention may work through a variety of mechanisms including, but not limited to, inhibiting proteolysis of the extracellular matrix, blocking the function of endothelial cell-extracellular matrix adhesion molecules, by antagonizing the function of angiogenesis inducers such as growth factors, and inhibiting integrin receptors expressed on proliferating endothelial cells. Examples of anti-angiogenic inhibitors that interfere with extracellular matrix proteolysis and which may be
 35 administered in combination with the compositions of the invention include, but are not limited to, AG-3340 (Agouron, La Jolla, CA), BAY-12-9566 (Bayer, West Haven, CT), BMS-275291 (Bristol Myers Squibb, Princeton, NJ), CGS-27032A (Novartis, East Hanover, NJ), Marimastat

(British Biotech, Oxford, UK), and Metastat (Aeterna, St-Foy, Quebec). Examples of anti-angiogenic inhibitors that act by blocking the function of endothelial cell-extracellular matrix adhesion molecules and which may be administered in combination with the compositions of the invention include, but are not limited to, EMD-121974 (Merck KGaA Darmstadt, Germany) and
5 Vitaxin (Ixsys, La Jolla, CA/Medimmune, Gaithersburg, MD). Examples of anti-angiogenic agents that act by directly antagonizing or inhibiting angiogenesis inducers and which may be administered in combination with the compositions of the invention include, but are not limited to, Angiozyme (Ribozyme, Boulder, CO), Anti-VEGF antibody (Genentech, S. San Francisco, CA), PTK-787/ZK-225846 (Novartis, Basel, Switzerland), SU-101 (Sugen, S. San Francisco, CA), SU-
10 5416 (Sugen/ Pharmacia Upjohn, Bridgewater, NJ), and SU-6668 (Sugen). Other anti-angiogenic agents act to indirectly inhibit angiogenesis. Examples of indirect inhibitors of angiogenesis which may be administered in combination with the compositions of the invention include, but are not limited to, IM-862 (Cytran, Kirkland, WA), Interferon-alpha, IL-12 (Roche, Nutley, NJ), and Pentosan polysulfate (Georgetown University, Washington, DC).

15 In particular embodiments, the use of compositions of the invention in combination with anti-angiogenic agents is contemplated for the treatment, prevention, and/or amelioration of an autoimmune disease, such as for example, an autoimmune disease described herein.

In a particular embodiment, the use of compositions of the invention in combination with anti-angiogenic agents is contemplated for the treatment, prevention, and/or amelioration of
20 arthritis. In a more particular embodiment, the use of compositions of the invention in combination with anti-angiogenic agents is contemplated for the treatment, prevention, and/or amelioration of rheumatoid arthritis.

In another embodiment, the polynucleotides encoding a polypeptide of the present invention are administered in combination with an angiogenic protein, or polynucleotides
25 encoding an angiogenic protein. Examples of angiogenic proteins that may be administered with the compositions of the invention include, but are not limited to, acidic and basic fibroblast growth factors, VEGF-1, VEGF-2, VEGF-3, epidermal growth factor alpha and beta, platelet-derived endothelial cell growth factor, platelet-derived growth factor, tumor necrosis factor alpha, hepatocyte growth factor, insulin-like growth factor, colony stimulating factor, macrophage colony
30 stimulating factor, granulocyte/macrophage colony stimulating factor, and nitric oxide synthase.

In additional embodiments, compositions of the invention are administered in combination with a chemotherapeutic agent. Chemotherapeutic agents that may be administered with the Therapeutics of the invention include, but are not limited to alkylating agents such as nitrogen
35 mustards (for example, Mechlorethamine, cyclophosphamide, Cyclophosphamide Ifosfamide, Melphalan (L-sarcolysin), and Chlorambucil), ethylenimines and methylmelamines (for example, Hexamethylmelamine and Thiotepe), alkyl sulfonates (for example, Busulfan), nitrosoureas (for example, Carmustine (BCNU), Lomustine (CCNU), Semustine (methyl-CCNU), and Streptozocin

(streptozotocin)), triazenes (for example, Dacarbazine (DTIC; dimethyltriazenoimidazolecarboxamide)), folic acid analogs (for example, Methotrexate (amethopterin)), pyrimidine analogs (for example, Fluorouracil (5-fluorouracil; 5-FU), Floxuridine (fluorodeoxyuridine; FudR), and Cytarabine (cytosine arabinoside)), purine analogs and related
5 inhibitors (for example, Mercaptopurine (6-mercaptopurine; 6-MP), Thioguanine (6-thioguanine; TG), and Pentostatin (2'-deoxycoformycin)), vinca alkaloids (for example, Vinblastine (VLB, vinblastine sulfate)) and Vincristine (vincristine sulfate)), epipodophyllotoxins (for example, Etoposide and Teniposide), antibiotics (for example, Dactinomycin (actinomycin D), Daunorubicin (daunomycin; rubidomycin), Doxorubicin, Bleomycin, Plicamycin (mithramycin),
10 and Mitomycin (mitomycin C), enzymes (for example, L-Asparaginase), biological response modifiers (for example, Interferon-alpha and interferon-alpha-2b), platinum coordination compounds (for example, Cisplatin (cis-DDP) and Carboplatin), anthracenedione (Mitoxantrone), substituted ureas (for example, Hydroxyurea), methylhydrazine derivatives (for example, Procarbazine (N-methylhydrazine; MIH), adrenocorticosteroids (for example, Prednisone),
15 progestins (for example, Hydroxyprogesterone caproate, Medroxyprogesterone, Medroxyprogesterone acetate, and Megestrol acetate), estrogens (for example, Diethylstilbestrol (DES), Diethylstilbestrol diphosphate, Estradiol, and Ethinyl estradiol), antiestrogens (for example, Tamoxifen), androgens (Testosterone propionate, and Fluoxymesterone), antiandrogens (for example, Flutamide), gonadotropin-releasing hormone analogs (for example, Leuprolide),
20 other hormones and hormone analogs (for example, methyltestosterone, estramustine, estramustine phosphate sodium, chlorotrianisene, and testolactone), and others (for example, dicarbazine, glutamic acid, and mitotane).

In one embodiment, the compositions of the invention are administered in combination with one or more of the following drugs: infliximab (also known as Remicade™ Centocor, Inc.),
25 Trocade (Roche, RO-32-3555), Leflunomide (also known as Arava™ from Hoechst Marion Roussel), Kineret™ (an IL-1 Receptor antagonist also known as Anakinra from Amgen, Inc.)

In a specific embodiment, compositions of the invention are administered in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or combination of one or more of the components of CHOP. In one embodiment, the compositions of the invention are
30 administered in combination with anti-CD20 antibodies, human monoclonal anti-CD20 antibodies. In another embodiment, the compositions of the invention are administered in combination with anti-CD20 antibodies and CHOP, or anti-CD20 antibodies and any combination of one or more of the components of CHOP, particularly cyclophosphamide and/or prednisone. In a specific embodiment, compositions of the invention are administered in combination with Rituximab. In a
35 further embodiment, compositions of the invention are administered with Rituximab and CHOP, or Rituximab and any combination of one or more of the components of CHOP, particularly cyclophosphamide and/or prednisone. In a specific embodiment, compositions of the invention are

administered in combination with tositumomab. In a further embodiment, compositions of the invention are administered with tositumomab and CHOP, or tositumomab and any combination of one or more of the components of CHOP, particularly cyclophosphamide and/or prednisone. The anti-CD20 antibodies may optionally be associated with radioisotopes, toxins or cytotoxic
5 prodrugs.

In another specific embodiment, the compositions of the invention are administered in combination Zevalin™. In a further embodiment, compositions of the invention are administered with Zevalin™ and CHOP, or Zevalin™ and any combination of one or more of the components of CHOP, particularly cyclophosphamide and/or prednisone. Zevalin™ may be associated with one
10 or more radisotopes. Particularly preferred isotopes are ⁹⁰Y and ¹¹¹In.

In an additional embodiment, the Therapeutics of the invention are administered in combination with cytokines. Cytokines that may be administered with the Therapeutics of the invention include, but are not limited to, IL2, IL3, IL4, IL5, IL6, IL7, IL10, IL12, IL13, IL15, anti-CD40, CD40L, IFN-gamma and TNF-alpha. In another embodiment, Therapeutics of the
15 invention may be administered with any interleukin, including, but not limited to, IL-1alpha, IL-1beta, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IL-16, IL-17, IL-18, IL-19, IL-20, and IL-21.

In one embodiment, the Therapeutics of the invention are administered in combination with members of the TNF family. TNF, TNF-related or TNF-like molecules that may be
20 administered with the Therapeutics of the invention include, but are not limited to, soluble forms of TNF-alpha, lymphotoxin-alpha (LT-alpha, also known as TNF-beta), LT-beta (found in complex heterotrimer LT-alpha2-beta), OPGL, FasL, CD27L, CD30L, CD40L, 4-1BBL, DcR3, OX40L, TNF-gamma (International Publication No. WO 96/14328), AIM-1 (International Publication No. WO 97/33899), endokine-alpha (International Publication No. WO 98/07880),
25 OPG, and neutrokin-alpha (International Publication No. WO 98/18921, OX40, and nerve growth factor (NGF), and soluble forms of Fas, CD30, CD27, CD40 and 4-1BB, TR2 (International Publication No. WO 96/34095), DR3 (International Publication No. WO 97/33904), DR4 (International Publication No. WO 98/32856), TR5 (International Publication No. WO 98/30693), TRANK, TR9 (International Publication No. WO 98/56892), TR10 (International Publication No.
30 WO 98/54202), 312C2 (International Publication No. WO 98/06842), and TR12, and soluble forms CD154, CD70, and CD153.

In an additional embodiment, the Therapeutics of the invention are administered in combination with angiogenic proteins. Angiogenic proteins that may be administered with the Therapeutics of the invention include, but are not limited to, Glioma Derived Growth Factor
35 (GDGF), as disclosed in European Patent Number EP-399816; Platelet Derived Growth Factor-A (PDGF-A), as disclosed in European Patent Number EP-682110; Platelet Derived Growth Factor-

B (PDGF-B), as disclosed in European Patent Number EP-282317; Placental Growth Factor (PIGF), as disclosed in International Publication Number WO 92/06194; Placental Growth Factor-2 (PIGF-2), as disclosed in Hauser et al., Growth Factors, 4:259-268 (1993); Vascular Endothelial Growth Factor (VEGF), as disclosed in International Publication Number WO 90/13649; Vascular
5 Endothelial Growth Factor-A (VEGF-A), as disclosed in European Patent Number EP-506477; Vascular Endothelial Growth Factor-2 (VEGF-2), as disclosed in International Publication Number WO 96/39515; Vascular Endothelial Growth Factor B (VEGF-3); Vascular Endothelial Growth Factor B-186 (VEGF-B186), as disclosed in International Publication Number WO 96/26736; Vascular Endothelial Growth Factor-D (VEGF-D), as disclosed in International
10 Publication Number WO 98/02543; Vascular Endothelial Growth Factor-D (VEGF-D), as disclosed in International Publication Number WO 98/07832; and Vascular Endothelial Growth Factor-E (VEGF-E), as disclosed in German Patent Number DE19639601. The above mentioned references are herein incorporated by reference in their entireties.

In an additional embodiment, the Therapeutics of the invention are administered in
15 combination with Fibroblast Growth Factors. Fibroblast Growth Factors that may be administered with the Therapeutics of the invention include, but are not limited to, FGF-1, FGF-2, FGF-3, FGF-4, FGF-5, FGF-6, FGF-7, FGF-8, FGF-9, FGF-10, FGF-11, FGF-12, FGF-13, FGF-14, and FGF-15.

In an additional embodiment, the Therapeutics of the invention are administered in
20 combination with hematopoietic growth factors. Hematopoietic growth factors that may be administered with the Therapeutics of the invention include, but are not limited to, granulocyte macrophage colony stimulating factor (GM-CSF) (sargramostim, LEUKINE™, PROKINE™), granulocyte colony stimulating factor (G-CSF) (filgrastim, NEUPOGEN™), macrophage colony stimulating factor (M-CSF, CSF-1) erythropoietin (epoetin alfa, EPOGEN™, PROCRIT™), stem
25 cell factor (SCF, c-kit ligand, steel factor), megakaryocyte colony stimulating factor, PIXY321 (a GMCSF/IL-3 fusion protein), interleukins, especially any one or more of IL-1 through IL-12, interferon-gamma, or thrombopoietin.

In certain embodiments, Therapeutics of the present invention are administered in
combination with adrenergic blockers, such as, for example, acebutolol, atenolol, betaxolol,
30 bisoprolol, carteolol, labetalol, metoprolol, nadolol, oxprenolol, penbutolol, pindolol, propranolol, sotalol, and timolol.

In another embodiment, the Therapeutics of the invention are administered in combination
with an antiarrhythmic drug (e.g., adenosine, amidoarone, bretylium, digitalis, digoxin, digitoxin,
diltiazem, disopyramide, esmolol, flecainide, lidocaine, mexiletine, moricizine, phenytoin,
35 procainamide, N-acetyl procainamide, propafenone, propranolol, quinidine, sotalol, tocainide, and verapamil).

In another embodiment, the Therapeutics of the invention are administered in combination with diuretic agents, such as carbonic anhydrase-inhibiting agents (e.g., acetazolamide, dichlorphenamide, and methazolamide), osmotic diuretics (e.g., glycerin, isosorbide, mannitol, and urea), diuretics that inhibit $\text{Na}^+\text{-K}^+\text{-2Cl}^-$ symport (e.g., furosemide, bumetanide, azosemide, 5 piretanide, tripamide, ethacrynic acid, muzolimine, and torsemide), thiazide and thiazide-like diuretics (e.g., bendroflumethiazide, benzthiazide, chlorothiazide, hydrochlorothiazide, hydroflumethiazide, methyclothiazide, polythiazide, trichormethiazide, chlorthalidone, indapamide, metolazone, and quinethazone), potassium sparing diuretics (e.g., amiloride and triamterene), and mineralcorticoid receptor antagonists (e.g., spironolactone, canrenone, and 10 potassium canrenoate).

In one embodiment, the Therapeutics of the invention are administered in combination with treatments for endocrine and/or hormone imbalance disorders. Treatments for endocrine and/or hormone imbalance disorders include, but are not limited to, ^{127}I , radioactive isotopes of iodine such as ^{131}I and ^{123}I ; recombinant growth hormone, such as HUMATROPE™ (recombinant 15 somatotropin); growth hormone analogs such as PROTROPIN™ (somatrem); dopamine agonists such as PARLODEL™ (bromocriptine); somatostatin analogs such as SANDOSTATIN™ (octreotide); gonadotropin preparations such as PREGNYL™, A.P.L.™ and PROFASI™ (chorionic gonadotropin (CG)), PERGONAL™ (menotropins), and METRODIN™ (urofollitropin (uFSH)); synthetic human gonadotropin releasing hormone preparations such as FACTREL™ and 20 LUTREPULSE™ (gonadorelin hydrochloride); synthetic gonadotropin agonists such as LUPRON™ (leuprolide acetate), SUPPRELIN™ (histrelin acetate), SYNAREL™ (nafarelin acetate), and ZOLADEX™ (goserelin acetate); synthetic preparations of thyrotropin-releasing hormone such as RELEFACT TRH™ and THYPINONE™ (protirelin); recombinant human TSH such as THYROGEN™; synthetic preparations of the sodium salts of the natural isomers of 25 thyroid hormones such as L-T₄™, SYNTHROID™ and LEVOTHROID™ (levothyroxine sodium), L-T₃™, CYTOMEL™ and TRIOSTAT™ (liothyroine sodium), and THYROLAR™ (liotrix); antithyroid compounds such as 6-*n*-propylthiouracil (propylthiouracil), 1-methyl-2-mercaptoimidazole and TAPAZOLE™ (methimazole), NEO-MERCAZOLE™ (carbimazole); beta-adrenergic receptor antagonists such as propranolol and esmolol; Ca²⁺ channel blockers; 30 dexamethasone and iodinated radiological contrast agents such as TELEPAQUE™ (iopanoic acid) and ORAGRAFIN™ (sodium ipodate).

Additional treatments for endocrine and/or hormone imbalance disorders include, but are not limited to, estrogens or conjugated estrogens such as ESTRACE™ (estradiol), ESTINYL™ (ethinyl estradiol), PREMARIN™, ESTRATAB™, ORTHO-EST™, OGEN™ and estropipate 35 (estrone), ESTROVIS™ (quinestrol), ESTRADERM™ (estradiol), DELESTROGEN™ and

VALERGEN™ (estradiol valerate), DEPO-ESTRADIOL CYPIONATE™ and ESTROJECT LA™ (estradiol cypionate); antiestrogens such as NOLVADEX™ (tamoxifen), SEROPHENE™ and CLOMID™ (clomiphene); progestins such as DURALUTIN™ (hydroxyprogesterone caproate), MPA™ and DEPO-PROVERA™ (medroxyprogesterone acetate), PROVERA™ and CYCRIN™
 5 (MPA), MEGACE™ (megestrol acetate), NORLUTIN™ (norethindrone), and NORLUTATE™ and AYGESTIN™ (norethindrone acetate); progesterone implants such as NORPLANT SYSTEM™ (subdermal implants of norgestrel); antiprogestins such as RU 486™ (mifepristone); hormonal contraceptives such as ENOVID™ (norethynodrel plus mestranol), PROGESTASERT™ (intrauterine device that releases progesterone), LOESTRIN™, BREVICON™, MODICON™,
 10 GENORA™, NELONA™, NORINYL™, OVACON-35™ and OVACON-50™ (ethinyl estradiol/norethindrone), LEVLEN™, NORDETTE™, TRI-LEVLEN™ and TRIPHASIL-21™ (ethinyl estradiol/levonorgestrel) LO/OVRAL™ and OVRAL™ (ethinyl estradiol/norgestrel), DEMULEN™ (ethinyl estradiol/ethynodiol diacetate), NORINYL™, ORTHO-NOVUM™, NORETHIN™, GENORA™, and NELOVA™ (norethindrone/mestranol), DESOGEN™ and
 15 ORTHO-CEPT™ (ethinyl estradiol/desogestrel), ORTHO-CYCLEN™ and ORTHO-TRICYCLEN™ (ethinyl estradiol/norgestimate), MICRONOR™ and NOR-QD™ (norethindrone), and OVRETTE™ (norgestrel).

Additional treatments for endocrine and/or hormone imbalance disorders include, but are not limited to, testosterone esters such as methenolone acetate and testosterone undecanoate;
 20 parenteral and oral androgens such as TESTOJECT-50™ (testosterone), TESTEX™ (testosterone propionate), DELATESTRYL™ (testosterone enanthate), DEPO-TESTOSTERONE™ (testosterone cypionate), DANOCRINE™ (danazol), HALOTESTIN™ (fluoxymesterone), ORETON METHYL™, TESTRED™ and VIRILON™ (methyltestosterone), and OXANDRIN™ (oxandrolone); testosterone transdermal systems such as TESTODERM™; androgen receptor
 25 antagonist and 5-alpha-reductase inhibitors such as ANDROCUR™ (cyproterone acetate), EULEXIN™ (flutamide), and PROSCAR™ (finasteride); adrenocorticotrophic hormone preparations such as CORTROSYN™ (cosyntropin); adrenocortical steroids and their synthetic analogs such as ACLOVATE™ (alclometasone dipropionate), CYCLOCORT™ (amcinonide), BECLOVENT™ and VANCERIL™ (beclomethasone dipropionate), CELESTONE™
 30 (betamethasone), BENISONE™ and UTICORT™ (betamethasone benzoate), DIPROSONE™ (betamethasone dipropionate), CELESTONE PHOSPHATE™ (betamethasone sodium phosphate), CELESTONE SOLUSPAN™ (betamethasone sodium phosphate and acetate), BETA-VAL™ and VALISONE™ (betamethasone valerate), TEMOVATE™ (clobetasol propionate), CLODERM™ (clocortolone pivalate), CORTEF™ and HYDROCORTONE™ (cortisol (hydrocortisone)),

HYDROCORTONE ACETATE™ (cortisol (hydrocortisone) acetate), LOCOID™ (cortisol (hydrocortisone) butyrate), HYDROCORTONE PHOSPHATE™ (cortisol (hydrocortisone) sodium phosphate), A-HYDROCORT™ and SOLU CORTEF™ (cortisol (hydrocortisone) sodium succinate), WESTCORT™ (cortisol (hydrocortisone) valerate), CORTISONE ACETATE™
 5 (cortisone acetate), DESOWEN™ and TRIDESILON™ (desonide), TOPICORT™ (desoximetasone), DECADRON™ (dexamethasone), DECADRON LA™ (dexamethasone acetate), DECADRON PHOSPHATE™ and HEXADROL PHOSPHATE™ (dexamethasone sodium phosphate), FLORONE™ and MAXIFLOR™ (diflorasone diacetate), FLORINEF ACETATE™ (fludrocortisone acetate), AEROBID™ and NASALIDE™ (flunisolide),
 10 FLUONID™ and SYNALAR™ (fluocinolone acetonide), LIDEX™ (fluocinonide), FLUOR-OP™ and FML™ (fluorometholone), CORDRAN™ (flurandrenolide), HALOG™ (halcinonide), HMS LIZUIFILM™ (medrysone), MEDROL™ (methylprednisolone), DEPO-MEDROL™ and MEDROL ACETATE™ (methylprednisone acetate), A-METHAPRED™ and SOLUMEDROL™ (methylprednisolone sodium succinate), ELOCON™ (mometasone furoate), HALDRONE™
 15 (paramethasone acetate), DELTA-CORTEF™ (prednisolone), ECONOPRED™ (prednisolone acetate), HYDELTRASOL™ (prednisolone sodium phosphate), HYDELTRA-T.B.A™ (prednisolone tebutate), DELTASONE™ (prednisone), ARISTOCORT™ and KENACORT™ (triamcinolone), KENALOG™ (triamcinolone acetonide), ARISTOCORT™ and KENACORT DIACETATE™ (triamcinolone diacetate), and ARISTOSPAN™ (triamcinolone hexacetonide);
 20 inhibitors of biosynthesis and action of adrenocortical steroids such as CYTADREN™ (aminogluthetimide), NIZORAL™ (ketoconazole), MODRASTANE™ (trilostane), and METOPIRONE™ (metyrapone); bovine, porcine or human insulin or mixtures thereof; insulin analogs; recombinant human insulin such as HUMULIN™ and NOVOLIN™; oral hypoglycemic agents such as ORAMIDE™ and ORINASE™ (tolbutamide), DIABINESE™ (chlorpropamide),
 25 TOLAMIDE™ and TOLINASE™ (tolazamide), DYMELOS™ (acetohexamide), glibenclamide, MICRONASE™, DIBETA™ and GLYNASE™ (glyburide), GLUCOTROL™ (glipizide), and DIAMICRON™ (gliclazide), GLUCOPHAGE™ (metformin), ciglitazone, pioglitazone, and alpha-glucosidase inhibitors; bovine or porcine glucagon; somatostatins such as SANDOSTATIN™ (octreotide); and diazoxides such as PROGLYCEM™ (diazoxide).

30 In one embodiment, the Therapeutics of the invention are administered in combination with treatments for uterine motility disorders. Treatments for uterine motility disorders include, but are not limited to, estrogen drugs such as conjugated estrogens (e.g., PREMARIN® and ESTRATAB®), estradiols (e.g., CLIMARA® and ALORA®), estropipate, and chlorotrianisene; progestin drugs (e.g., AMEN® (medroxyprogesterone), MICRONOR® (norethidrone acetate),
 35 PROMETRIUM® progesterone, and megestrol acetate); and estrogen/progesterone combination

therapies such as, for example, conjugated estrogens/medroxyprogesterone (e.g., PREMPRO™ and PREMPHASE®) and norethindrone acetate/ethinyl estsradiol (e.g., FEMHRT™).

In an additional embodiment, the Therapeutics of the invention are administered in combination with drugs effective in treating iron deficiency and hypochromic anemias, including
5 but not limited to, ferrous sulfate (iron sulfate, FEOSOL™), ferrous fumarate (e.g., FEOSTAT™), ferrous gluconate (e.g., FERGON™), polysaccharide-iron complex (e.g., NIFEREX™), iron dextran injection (e.g., INFED™), cupric sulfate, pyroxidine, riboflavin, Vitamin B₁₂, cyanocobalamin injection (e.g., REDISOL™, RUBRAMIN PC™), hydroxocobalamin, folic acid (e.g., FOLVITE™), leucovorin (folinic acid, 5-CHOH4PteGlu, citrovorum factor) or
10 WELLCOVORIN (Calcium salt of leucovorin), transferrin or ferritin.

In certain embodiments, the Therapeutics of the invention are administered in combination with agents used to treat psychiatric disorders. Psychiatric drugs that may be administered with the Therapeutics of the invention include, but are not limited to, antipsychotic agents (e.g., chlorpromazine, chlorprothixene, clozapine, fluphenazine, haloperidol, loxapine, mesoridazine,
15 molindone, olanzapine, perphenazine, pimozide, quetiapine, risperidone, thioridazine, thiothixene, trifluoperazine, and triflupromazine), antimanic agents (e.g., carbamazepine, divalproex sodium, lithium carbonate, and lithium citrate), antidepressants (e.g., amitriptyline, amoxapine, bupropion, citalopram, clomipramine, desipramine, doxepin, fluvoxamine, fluoxetine, imipramine, isocarboxazid, maprotiline, mirtazapine, nefazodone, nortriptyline, paroxetine, phenelzine,
20 protriptyline, sertraline, tranlycypromine, trazodone, trimipramine, and venlafaxine), antianxiety agents (e.g., alprazolam, buspirone, chlordiazepoxide, clorazepate, diazepam, halazepam, lorazepam, oxazepam, and prazepam), and stimulants (e.g., d-amphetamine, methylphenidate, and pemoline).

In other embodiments, the Therapeutics of the invention are administered in combination
25 with agents used to treat neurological disorders. Neurological agents that may be administered with the Therapeutics of the invention include, but are not limited to, antiepileptic agents (e.g., carbamazepine, clonazepam, ethosuximide, phenobarbital, phenytoin, primidone, valproic acid, divalproex sodium, felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate, zonisamide, diazepam, lorazepam, and clonazepam), antiparkinsonian agents (e.g.,
30 levodopa/carbidopa, selegiline, amantidine, bromocriptine, pergolide, ropinirole, pramipexole, benztropine; biperiden; ethopropazine; procyclidine; trihexyphenidyl, tolcapone), and ALS therapeutics (e.g. riluzole).

In another embodiment, Therapeutics of the invention are administered in combination with vasodilating agents and/or calcium channel blocking agents. Vasodilating agents that may be
35 administered with the Therapeutics of the invention include, but are not limited to, Angiotensin Converting Enzyme (ACE) inhibitors (e.g., papaverine, isoxsuprine, benazepril, captopril,

cilazapril, enalapril, enalaprilat, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, spirapril, trandolapril, and nylidrin), and nitrates (e.g., isosorbide dinitrate, isosorbide mononitrate, and nitroglycerin). Examples of calcium channel blocking agents that may be administered in combination with the Therapeutics of the invention include, but are not limited to amlodipine, bepridil, diltiazem, felodipine, flunarizine, isradipine, nicardipine, nifedipine, nimodipine, and verapamil.

In certain embodiments, the Therapeutics of the invention are administered in combination with treatments for gastrointestinal disorders. Treatments for gastrointestinal disorders that may be administered with the Therapeutic of the invention include, but are not limited to, H₂ histamine receptor antagonists (e.g., TAGAMETTM (cimetidine), ZANTACTM (ranitidine), PEPCIDTM (famotidine), and AXIDTM (nizatidine)); inhibitors of H⁺, K⁺ ATPase (e.g., PREVACIDTM (lansoprazole) and PRILOSECTM (omeprazole)); Bismuth compounds (e.g., PEPTO-BISMOLTM (bismuth subsalicylate) and DE-NOLTM (bismuth subcitrate)); various antacids; sucralfate; prostaglandin analogs (e.g., CYTOTECHTM (misoprostol)); muscarinic cholinergic antagonists; laxatives (e.g., surfactant laxatives, stimulant laxatives, saline and osmotic laxatives); antidiarrheal agents (e.g., LOMOTILTM (diphenoxylate), MOTOFENTM (diphenoxin), and IMODIUMTM (loperamide hydrochloride)), synthetic analogs of somatostatin such as SANDOSTATINTM (octreotide), antiemetic agents (e.g., ZOFTRANTM (ondansetron), KYTRILTM (granisetron hydrochloride), tropisetron, dolasetron, metoclopramide, chlorpromazine, perphenazine, prochlorperazine, promethazine, thiethylperazine, trifluorpromazine, domperidone, haloperidol, droperidol, trimethobenzamide, dexamethasone, methylprednisolone, dronabinol, and nabilone); D2 antagonists (e.g., metoclopramide, trimethobenzamide and chlorpromazine); bile salts; chenodeoxycholic acid; ursodeoxycholic acid; and pancreatic enzyme preparations such as pancreatin and pancrelipase.

In additional embodiments, the Therapeutics of the invention are administered in combination with other therapeutic or prophylactic regimens, such as, for example, radiation therapy.

Example 14: Method of Treating Decreased Levels of the Polypeptide

The present invention relates to a method for treating an individual in need of an increased level of a polypeptide of the invention in the body comprising administering to such an individual a composition comprising a therapeutically effective amount of polypeptides (including agonists thereto), and/or antibodies of the invention. Moreover, it will be appreciated that conditions caused by a decrease in the standard or normal expression level of a polypeptide of the present

invention in an individual may be treated by administering agonists of said polypeptide. Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a Therapeutic comprising an amount of the agonist (including polypeptides and antibodies of the present invention) to increase the activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily dose 0.1-100 ug/kg of the agonist for six consecutive days. The exact details of the dosing scheme, based on administration and formulation, are provided in Example 13.

Example 15: Method of Treating Increased Levels of the Polypeptide

The present invention also relates to a method of treating an individual in need of a decreased level of a polypeptide of the invention in the body comprising administering to such an individual a composition comprising a therapeutically effective amount of an antagonist of the invention (including polypeptides and antibodies of the invention).

In one example, antisense technology is used to inhibit production of a polypeptide of the present invention. This technology is one example of a method of decreasing levels of a polypeptide, due to a variety of etiologies, such as cancer.

For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the treatment was well tolerated. The antisense polynucleotides of the present invention can be formulated using techniques and formulations described herein (e.g. see Example 13), or otherwise known in the art.

Example 16: Method of Treatment Using Gene Therapy-Ex Vivo

One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e.g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37 degree C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer is trypsinized and scaled into larger flasks.

5 pMV-7 (Kirschmeier, P.T. et al., DNA, 7:219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

10 The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5' and 3' end sequences respectively as set forth in Example 1 using primers and having appropriate restriction sites and initiation/stop codons, if necessary. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

15 The amphotropic pA317 or GP+am12 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

20 Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media. If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

30 The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads.

**Example 17: Gene Therapy Using Endogenous Genes Corresponding To
Polynucleotides of the Invention**

Another method of gene therapy according to the present invention involves operably
5 associating the endogenous polynucleotide sequence of the invention with a promoter via
homologous recombination as described, for example, in U.S. Patent NO: 5,641,670, issued June
24, 1997; International Publication NO: WO 96/29411, published September 26, 1996;
International Publication NO: WO 94/12650, published August 4, 1994; Koller et al., *Proc. Natl.
Acad. Sci. USA*, 86:8932-8935 (1989); and Zijlstra et al., *Nature*, 342:435-438 (1989). This
10 method involves the activation of a gene which is present in the target cells, but which is not
expressed in the cells, or is expressed at a lower level than desired.

Polynucleotide constructs are made which contain a promoter and targeting sequences,
which are homologous to the 5' non-coding sequence of endogenous polynucleotide sequence,
flanking the promoter. The targeting sequence will be sufficiently near the 5' end of the
15 polynucleotide sequence so the promoter will be operably linked to the endogenous sequence upon
homologous recombination. The promoter and the targeting sequences can be amplified using
PCR. Preferably, the amplified promoter contains distinct restriction enzyme sites on the 5' and 3'
ends. Preferably, the 3' end of the first targeting sequence contains the same restriction enzyme
site as the 5' end of the amplified promoter and the 5' end of the second targeting sequence
20 contains the same restriction site as the 3' end of the amplified promoter.

The amplified promoter and the amplified targeting sequences are digested with the
appropriate restriction enzymes and subsequently treated with calf intestinal phosphatase. The
digested promoter and digested targeting sequences are added together in the presence of T4 DNA
ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two
25 fragments. The construct is size fractionated on an agarose gel, then purified by phenol extraction
and ethanol precipitation.

In this Example, the polynucleotide constructs are administered as naked polynucleotides
via electroporation. However, the polynucleotide constructs may also be administered with
transfection-facilitating agents, such as liposomes, viral sequences, viral particles, precipitating
30 agents, etc. Such methods of delivery are known in the art.

Once the cells are transfected, homologous recombination will take place which results in
the promoter being operably linked to the endogenous polynucleotide sequence. This results in the
expression of polynucleotide corresponding to the polynucleotide in the cell. Expression may be
detected by immunological staining, or any other method known in the art.

35 Fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in
DMEM + 10% fetal calf serum. Exponentially growing or early stationary phase fibroblasts are
trypsinized and rinsed from the plastic surface with nutrient medium. An aliquot of the cell

suspension is removed for counting, and the remaining cells are subjected to centrifugation. The supernatant is aspirated and the pellet is resuspended in 5 ml of electroporation buffer (20 mM HEPES pH 7.3, 137 mM NaCl, 5 mM KCl, 0.7 mM Na₂ HPO₄, 6 mM dextrose). The cells are recentrifuged, the supernatant aspirated, and the cells resuspended in electroporation buffer containing 1 mg/ml acetylated bovine serum albumin. The final cell suspension contains approximately 3X10⁶ cells/ml. Electroporation should be performed immediately following resuspension.

Plasmid DNA is prepared according to standard techniques. For example, to construct a plasmid for targeting to the locus corresponding to the polynucleotide of the invention, plasmid pUC18 (MBI Fermentas, Amherst, NY) is digested with HindIII. The CMV promoter is amplified by PCR with an XbaI site on the 5' end and a BamHI site on the 3' end. Two non-coding sequences are amplified via PCR: one non-coding sequence (fragment 1) is amplified with a HindIII site at the 5' end and an Xba site at the 3' end; the other non-coding sequence (fragment 2) is amplified with a BamHI site at the 5' end and a HindIII site at the 3' end. The CMV promoter and the fragments (1 and 2) are digested with the appropriate enzymes (CMV promoter - XbaI and BamHI; fragment 1 - XbaI; fragment 2 - BamHI) and ligated together. The resulting ligation product is digested with HindIII, and ligated with the HindIII-digested pUC18 plasmid.

Plasmid DNA is added to a sterile cuvette with a 0.4 cm electrode gap (Bio-Rad). The final DNA concentration is generally at least 120 µg/ml. 0.5 ml of the cell suspension (containing approximately 1.5X10⁶ cells) is then added to the cuvette, and the cell suspension and DNA solutions are gently mixed. Electroporation is performed with a Gene-Pulser apparatus (Bio-Rad). Capacitance and voltage are set at 960 µF and 250-300 V, respectively. As voltage increases, cell survival decreases, but the percentage of surviving cells that stably incorporate the introduced DNA into their genome increases dramatically. Given these parameters, a pulse time of approximately 14-20 mSec should be observed.

Electroporated cells are maintained at room temperature for approximately 5 min, and the contents of the cuvette are then gently removed with a sterile transfer pipette. The cells are added directly to 10 ml of prewarmed nutrient media (DMEM with 15% calf serum) in a 10 cm dish and incubated at 37 degree C. The following day, the media is aspirated and replaced with 10 ml of fresh media and incubated for a further 16-24 hours.

The engineered fibroblasts are then injected into the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads. The fibroblasts now produce the protein product. The fibroblasts can then be introduced into a patient as described above.

Example 18: Method of Treatment Using Gene Therapy - In Vivo

Another aspect of the present invention is using *in vivo* gene therapy methods to prevent,

treat, and/or ameliorate cancer or other hyperproliferative diseases and disorders. The gene therapy method relates to the introduction of naked nucleic acid (DNA, RNA, and antisense DNA or RNA) sequences into an animal to increase or decrease the expression of the polypeptide. The polynucleotide of the present invention may be operatively linked to (i.e., associated with) a promoter or any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques and methods are known in the art, see, for example, WO90/11092, WO98/11779; U.S. Patent NO. 5693622, 5705151, 5580859; Tabata et al., *Cardiovasc. Res.* 35(3):470-479 (1997); Chao et al., *Pharmacol. Res.* 35(6):517-522 (1997); Wolff, *Neuromuscul. Disord.* 7(5):314-318 (1997); Schwartz et al., *Gene Ther.* 3(5):405-411 (1996); Tsurumi et al., *Circulation* 94(12):3281-3290 (1996) (incorporated herein by reference).

The polynucleotide constructs may be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, intestine and the like). The polynucleotide constructs can be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

The term "naked" polynucleotide, DNA or RNA, refers to sequences that are free from any delivery vehicle that acts to assist, promote, or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotides of the present invention may also be delivered in liposome formulations (such as those taught in Felgner P.L. et al. (1995) *Ann. NY Acad. Sci.* 772:126-139 and Abdallah B. et al. (1995) *Biol. Cell* 85(1):1-7) which can be prepared by methods well known to those skilled in the art.

The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Any strong promoter known to those skilled in the art can be used for driving the expression of DNA. Unlike other gene therapy techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct can be delivered to the interstitial space of tissues within an animal, including muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed

below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. *In vivo* muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked polynucleotide injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 g/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration. The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked polynucleotide constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The dose response effects of injected polynucleotide in muscle *in vivo* is determined as follows. Suitable template DNA for production of mRNA coding for polypeptide of the present invention is prepared in accordance with a standard recombinant DNA methodology. The template DNA, which may be either circular or linear, is either used as naked DNA or complexed with liposomes. The quadriceps muscles of mice are then injected with various amounts of the template DNA.

Five to six week old female and male Balb/C mice are anesthetized by intraperitoneal injection with 0.3 ml of 2.5% Avertin. A 1.5 cm incision is made on the anterior thigh, and the quadriceps muscle is directly visualized. The template DNA is injected in 0.1 ml of carrier in a 1 cc syringe through a 27 gauge needle over one minute, approximately 0.5 cm from the distal insertion site of the muscle into the knee and about 0.2 cm deep. A suture is placed over the injection site for future localization, and the skin is closed with stainless steel clips.

After an appropriate incubation time (e.g., 7 days) muscle extracts are prepared by excising the entire quadriceps. Every fifth 15 um cross-section of the individual quadriceps muscles is histochemically stained for protein expression. A time course for protein expression may be done in a similar fashion except that quadriceps from different mice are harvested at different times. Persistence of DNA in muscle following injection may be determined by Southern blot analysis after preparing total cellular DNA and HIRT supernatants from injected and control mice. The results of the above experimentation in mice can be used to extrapolate proper dosages and other treatment parameters in humans and other animals using naked DNA.

Example 19: Transgenic Animals

5 The polypeptides of the invention can also be expressed in transgenic animals. Animals of any species, including, but not limited to, mice, rats, rabbits, hamsters, guinea pigs, pigs, micro-pigs, goats, sheep, cows and non-human primates, *e.g.*, baboons, monkeys, and chimpanzees may be used to generate transgenic animals. In a specific embodiment, techniques described herein or otherwise known in the art, are used to express polypeptides of the invention in humans, as part of a gene therapy protocol.

10 Any technique known in the art may be used to introduce the transgene (*i.e.*, polynucleotides of the invention) into animals to produce the founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection (Paterson et al., Appl. Microbiol. Biotechnol. 40:691-698 (1994); Carver et al., Biotechnology (NY) 11:1263-1270 (1993); Wright et al., Biotechnology (NY) 9:830-834 (1991); and Hoppe et al., U.S. Pat. No. 15 4,873,191 (1989)); retrovirus mediated gene transfer into germ lines (Van der Putten et al., Proc. Natl. Acad. Sci., USA 82:6148-6152 (1985)), blastocysts or embryos; gene targeting in embryonic stem cells (Thompson et al., Cell 56:313-321 (1989)); electroporation of cells or embryos (Lo, 1983, Mol Cell. Biol. 3:1803-1814 (1983)); introduction of the polynucleotides of the invention using a gene gun (see, *e.g.*, Ulmer et al., Science 259:1745 (1993); introducing nucleic acid 20 constructs into embryonic pluripotent stem cells and transferring the stem cells back into the blastocyst; and sperm-mediated gene transfer (Lavitrano et al., Cell 57:717-723 (1989); etc. For a review of such techniques, see Gordon, "Transgenic Animals," Intl. Rev. Cytol. 115:171-229 (1989), which is incorporated by reference herein in its entirety.

Any technique known in the art may be used to produce transgenic clones containing 25 polynucleotides of the invention, for example, nuclear transfer into enucleated oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (Campell et al., Nature 380:64-66 (1996); Wilmut et al., Nature 385:810-813 (1997)).

The present invention provides for transgenic animals that carry the transgene in all their cells, as well as animals which carry the transgene in some, but not all their cells, *i.e.*, mosaic 30 animals or chimeric. The transgene may be integrated as a single transgene or as multiple copies such as in concatamers, *e.g.*, head-to-head tandems or head-to-tail tandems. The transgene may also be selectively introduced into and activated in a particular cell type by following, for example, the teaching of Lasko et al. (Lasko et al., Proc. Natl. Acad. Sci. USA 89:6232-6236 (1992)). The regulatory sequences required for such a cell-type specific activation will depend upon the 35 particular cell type of interest, and will be apparent to those of skill in the art. When it is desired that the polynucleotide transgene be integrated into the chromosomal site of the endogenous gene, gene targeting is preferred. Briefly, when such a technique is to be utilized, vectors containing

some nucleotide sequences homologous to the endogenous gene are designed for the purpose of integrating, via homologous recombination with chromosomal sequences, into and disrupting the function of the nucleotide sequence of the endogenous gene. The transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type, by following, for example, the teaching of Gu et al. (Gu et al., Science 265:103-106 (1994)). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the transgene has taken place. The level of mRNA expression of the transgene in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, *in situ* hybridization analysis, and reverse transcriptase-PCR (rt-PCR). Samples of transgenic gene-expressing tissue may also be evaluated immunocytochemically or immunohistochemically using antibodies specific for the transgene product.

Once the founder animals are produced, they may be bred, inbred, outbred, or crossbred to produce colonies of the particular animal. Examples of such breeding strategies include, but are not limited to: outbreeding of founder animals with more than one integration site in order to establish separate lines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous transgenic animals to produce animals homozygous for a given integration site in order to both augment expression and eliminate the need for screening of animals by DNA analysis; crossing of separate homozygous lines to produce compound heterozygous or homozygous lines; and breeding to place the transgene on a distinct background that is appropriate for an experimental model of interest.

Transgenic animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Example 20: Knock-Out Animals

Endogenous gene expression can also be reduced by inactivating or "knocking out" the gene and/or its promoter using targeted homologous recombination. (e.g., see Smithies et al., Nature 317:230-234 (1985); Thomas & Capecchi, Cell 51:503-512 (1987); Thompson et al., Cell 5:313-321 (1989); each of which is incorporated by reference herein in its entirety). For example,

a mutant, non-functional polynucleotide of the invention (or a completely unrelated DNA sequence) flanked by DNA homologous to the endogenous polynucleotide sequence (either the coding regions or regulatory regions of the gene) can be used, with or without a selectable marker and/or a negative selectable marker, to transfect cells that express polypeptides of the invention *in vivo*. In another embodiment, techniques known in the art are used to generate knockouts in cells that contain, but do not express the gene of interest. Insertion of the DNA construct, via targeted homologous recombination, results in inactivation of the targeted gene. Such approaches are particularly suited in research and agricultural fields where modifications to embryonic stem cells can be used to generate animal offspring with an inactive targeted gene (e.g., see Thomas & Capecchi 1987 and Thompson 1989, *supra*). However this approach can be routinely adapted for use in humans provided the recombinant DNA constructs are directly administered or targeted to the required site *in vivo* using appropriate viral vectors that will be apparent to those of skill in the art.

In further embodiments of the invention, cells that are genetically engineered to express the polypeptides of the invention, or alternatively, that are genetically engineered not to express the polypeptides of the invention (e.g., knockouts) are administered to a patient *in vivo*. Such cells may be obtained from the patient (i.e., animal, including human) or an MHC compatible donor and can include, but are not limited to fibroblasts, bone marrow cells, blood cells (e.g., lymphocytes), adipocytes, muscle cells, endothelial cells etc. The cells are genetically engineered *in vitro* using recombinant DNA techniques to introduce the coding sequence of polypeptides of the invention into the cells, or alternatively, to disrupt the coding sequence and/or endogenous regulatory sequence associated with the polypeptides of the invention, e.g., by transduction (using viral vectors, and preferably vectors that integrate the transgene into the cell genome) or transfection procedures, including, but not limited to, the use of plasmids, cosmids, YACs, naked DNA, electroporation, liposomes, etc. The coding sequence of the polypeptides of the invention can be placed under the control of a strong constitutive or inducible promoter or promoter/enhancer to achieve expression, and preferably secretion, of the polypeptides of the invention. The engineered cells which express and preferably secrete the polypeptides of the invention can be introduced into the patient systemically, e.g., in the circulation, or intraperitoneally.

Alternatively, the cells can be incorporated into a matrix and implanted in the body, e.g., genetically engineered fibroblasts can be implanted as part of a skin graft; genetically engineered endothelial cells can be implanted as part of a lymphatic or vascular graft. (See, for example, Anderson et al. U.S. Patent No. 5,399,349; and Mulligan & Wilson, U.S. Patent No. 5,460,959 each of which is incorporated by reference herein in its entirety).

When the cells to be administered are non-autologous or non-MHC compatible cells, they can be administered using well known techniques which prevent the development of a host immune response against the introduced cells. For example, the cells may be introduced in an

encapsulated form which, while allowing for an exchange of components with the immediate extracellular environment, does not allow the introduced cells to be recognized by the host immune system.

Transgenic and "knock-out" animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Example 21: Assays Detecting Stimulation or Inhibition of B cell Proliferation and Differentiation

Generation of functional humoral immune responses requires both soluble and cognate signaling between B-lineage cells and their microenvironment. Signals may impart a positive stimulus that allows a B-lineage cell to continue its programmed development, or a negative stimulus that instructs the cell to arrest its current developmental pathway. To date, numerous stimulatory and inhibitory signals have been found to influence B cell responsiveness including IL-2, IL-4, IL-5, IL-6, IL-7, IL10, IL-13, IL-14 and IL-15. Interestingly, these signals are by themselves weak effectors but can, in combination with various co-stimulatory proteins, induce activation, proliferation, differentiation, homing, tolerance and death among B cell populations.

One of the best studied classes of B-cell co-stimulatory proteins is the TNF-superfamily. Within this family CD40, CD27, and CD30 along with their respective ligands CD154, CD70, and CD153 have been found to regulate a variety of immune responses. Assays which allow for the detection and/or observation of the proliferation and differentiation of these B-cell populations and their precursors are valuable tools in determining the effects various proteins may have on these B-cell populations in terms of proliferation and differentiation. Listed below are two assays designed to allow for the detection of the differentiation, proliferation, or inhibition of B-cell populations and their precursors.

In Vitro Assay- Agonists or antagonists of the invention can be assessed for its ability to induce activation, proliferation, differentiation or inhibition and/or death in B-cell populations and their precursors. The activity of the agonists or antagonists of the invention on purified human tonsillar B cells, measured qualitatively over the dose range from 0.1 to 10,000 ng/mL, is assessed in a standard B-lymphocyte co-stimulation assay in which purified tonsillar B cells are cultured in the presence of either formalin-fixed *Staphylococcus aureus* Cowan I (SAC) or immobilized anti-human IgM antibody as the priming agent. Second signals such as IL-2 and IL-15 synergize with SAC and IgM crosslinking to elicit B cell proliferation as measured by tritiated-thymidine incorporation. Novel synergizing agents can be readily identified using this assay. The assay involves isolating human tonsillar B cells by magnetic bead (MACS) depletion of CD3-positive

cells. The resulting cell population is greater than 95% B cells as assessed by expression of CD45R(B220).

Various dilutions of each sample are placed into individual wells of a 96-well plate to which are added 10^5 B-cells suspended in culture medium (RPMI 1640 containing 10% FBS, 5×10^{-5} M 2ME, 100U/ml penicillin, 10ug/ml streptomycin, and 10^{-5} dilution of SAC) in a total volume of 150ul. Proliferation or inhibition is quantitated by a 20h pulse (1uCi/well) with 3H-thymidine (6.7 Ci/mM) beginning 72h post factor addition. The positive and negative controls are IL2 and medium respectively.

In vivo Assay- BALB/c mice are injected (i.p.) twice per day with buffer only, or 2 mg/Kg of agonists or antagonists of the invention, or truncated forms thereof. Mice receive this treatment for 4 consecutive days, at which time they are sacrificed and various tissues and serum collected for analyses. Comparison of H&E sections from normal spleens and spleens treated with agonists or antagonists of the invention identify the results of the activity of the agonists or antagonists on spleen cells, such as the diffusion of peri-arterial lymphatic sheaths, and/or significant increases in the nucleated cellularity of the red pulp regions, which may indicate the activation of the differentiation and proliferation of B-cell populations. Immunohistochemical studies using a B cell marker, anti-CD45R(B220), are used to determine whether any physiological changes to splenic cells, such as splenic disorganization, are due to increased B-cell representation within loosely defined B-cell zones that infiltrate established T-cell regions.

Flow cytometric analyses of the spleens from mice treated with agonist or antagonist is used to indicate whether the agonists or antagonists specifically increases the proportion of ThB+, CD45R(B220)dull B cells over that which is observed in control mice.

Likewise, a predicted consequence of increased mature B-cell representation *in vivo* is a relative increase in serum Ig titers. Accordingly, serum IgM and IgA levels are compared between buffer and agonists or antagonists-treated mice.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 22: T Cell Proliferation Assay

A CD3-induced proliferation assay is performed on PBMCs and is measured by the uptake of 3 H-thymidine. The assay is performed as follows. Ninety-six well plates are coated with 100 μ l/well of mAb to CD3 (HIT3a, Pharmingen) or isotype-matched control mAb (B33.1) overnight at 4 degrees C (1 μ g/ml in .05M bicarbonate buffer, pH 9.5), then washed three times with PBS. PBMC are isolated by F/H gradient centrifugation from human peripheral blood and added to quadruplicate wells (5×10^4 /well) of mAb coated plates in RPMI containing 10% FCS and P/S

the presence of varying concentrations of agonists or antagonists of the invention (total volume 200 μ l). Relevant protein buffer and medium alone are controls. After 48 hr. culture at 37 degrees C, plates are spun for 2 min. at 1000 rpm and 100 μ l of supernatant is removed and stored -20 degrees C for measurement of IL-2 (or other cytokines) if effect on proliferation is observed.

5 Wells are supplemented with 100 μ l of medium containing 0.5 μ Ci of 3 H-thymidine and cultured at 37 degrees C for 18-24 hr. Wells are harvested and incorporation of 3 H-thymidine used as a measure of proliferation. Anti-CD3 alone is the positive control for proliferation. IL-2 (100 U/ml) is also used as a control which enhances proliferation. Control antibody which does not induce proliferation of T cells is used as the negative control for the effects of agonists or antagonists of

10 the invention.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

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Example 23: Effect of Agonists or Antagonists of the Invention on the Expression of MHC Class II, Costimulatory and Adhesion Molecules and Cell Differentiation of Monocytes and Monocyte-Derived Human Dendritic Cells

20 Dendritic cells are generated by the expansion of proliferating precursors found in the peripheral blood: adherent PBMC or elutriated monocytic fractions are cultured for 7-10 days with GM-CSF (50 ng/ml) and IL-4 (20 ng/ml). These dendritic cells have the characteristic phenotype of immature cells (expression of CD1, CD80, CD86, CD40 and MHC class II antigens). Treatment with activating factors, such as TNF- α , causes a rapid change in surface phenotype (increased expression of

25 MHC class I and II, costimulatory and adhesion molecules, downregulation of FC γ RII, upregulation of CD83). These changes correlate with increased antigen-presenting capacity and with functional maturation of the dendritic cells.

FACS analysis of surface antigens is performed as follows. Cells are treated 1-3 days with increasing concentrations of agonist or antagonist of the invention or LPS (positive control), washed

30 with PBS containing 1% BSA and 0.02 mM sodium azide, and then incubated with 1:20 dilution of appropriate FITC- or PE-labeled monoclonal antibodies for 30 minutes at 4 degrees C. After an additional wash, the labeled cells are analyzed by flow cytometry on a FACScan (Becton Dickinson).

Effect on the production of cytokines. Cytokines generated by dendritic cells, in particular

35 IL-12, are important in the initiation of T-cell dependent immune responses. IL-12 strongly influences the development of Th1 helper T-cell immune response, and induces cytotoxic T and

NK cell function. An ELISA is used to measure the IL-12 release as follows. Dendritic cells ($10^6/\text{ml}$) are treated with increasing concentrations of agonists or antagonists of the invention for 24 hours. LPS (100 ng/ml) is added to the cell culture as positive control. Supernatants from the cell cultures are then collected and analyzed for IL-12 content using commercial ELISA kit (e.g.,
5 R & D Systems (Minneapolis, MN)). The standard protocols provided with the kits are used.

Effect on the expression of MHC Class II, costimulatory and adhesion molecules. Three major families of cell surface antigens can be identified on monocytes: adhesion molecules, molecules involved in antigen presentation, and Fc receptor. Modulation of the expression of
10 MHC class II antigens and other costimulatory molecules, such as B7 and ICAM-1, may result in changes in the antigen presenting capacity of monocytes and ability to induce T cell activation. Increased expression of Fc receptors may correlate with improved monocyte cytotoxic activity, cytokine release and phagocytosis.

FACS analysis is used to examine the surface antigens as follows. Monocytes are treated
15 1-5 days with increasing concentrations of agonists or antagonists of the invention or LPS (positive control), washed with PBS containing 1% BSA and 0.02 mM sodium azide, and then incubated with 1:20 dilution of appropriate FITC- or PE-labeled monoclonal antibodies for 30 minutes at 4 degrees C. After an additional wash, the labeled cells are analyzed by flow cytometry on a FACScan (Becton Dickinson).

20

Monocyte activation and/or increased survival. Assays for molecules that activate (or alternatively, inactivate) monocytes and/or increase monocyte survival (or alternatively, decrease monocyte survival) are known in the art and may routinely be applied to determine whether a molecule of the invention functions as an inhibitor or activator of monocytes. Agonists or
25 antagonists of the invention can be screened using the three assays described below. For each of these assays, Peripheral blood mononuclear cells (PBMC) are purified from single donor leukopacks (American Red Cross, Baltimore, MD) by centrifugation through a Histopaque gradient (Sigma). Monocytes are isolated from PBMC by counterflow centrifugal elutriation.

Monocyte Survival Assay. Human peripheral blood monocytes progressively lose viability when cultured in absence of serum or other stimuli. Their death results from internally regulated processes (apoptosis). Addition to the culture of activating factors, such as TNF-alpha dramatically improves cell survival and prevents DNA fragmentation. Propidium iodide (PI) staining is used to measure apoptosis as follows. Monocytes are cultured for 48 hours in
35 polypropylene tubes in serum-free medium (positive control), in the presence of 100 ng/ml TNF-alpha (negative control), and in the presence of varying concentrations of the compound to be tested. Cells are suspended at a concentration of $2 \times 10^6/\text{ml}$ in PBS containing PI at a final

concentration of 5 µg/ml, and then incubated at room temperature for 5 minutes before FACScan analysis. PI uptake has been demonstrated to correlate with DNA fragmentation in this experimental paradigm.

5 Effect on cytokine release. An important function of monocytes/macrophages is their regulatory activity on other cellular populations of the immune system through the release of cytokines after stimulation. An ELISA to measure cytokine release is performed as follows. Human monocytes are incubated at a density of 5×10^5 cells/ml with increasing concentrations of agonists or antagonists of the invention and under the same conditions, but in the absence of
10 agonists or antagonists. For IL-12 production, the cells are primed overnight with IFN (100 U/ml) in the presence of agonist or antagonist of the invention. LPS (10 ng/ml) is then added. Conditioned media are collected after 24h and kept frozen until use. Measurement of TNF-alpha, IL-10, MCP-1 and IL-8 is then performed using a commercially available ELISA kit (e.g., R & D Systems (Minneapolis, MN)) and applying the standard protocols provided with the kit.

15 Oxidative burst. Purified monocytes are plated in 96-w plate at 2×10^5 cell/well. Increasing concentrations of agonists or antagonists of the invention are added to the wells in a total volume of 0.2 ml culture medium (RPMI 1640 + 10% FCS, glutamine and antibiotics). After 3 days incubation, the plates are centrifuged and the medium is removed from the wells. To the
20 macrophage monolayers, 0.2 ml per well of phenol red solution (140 mM NaCl, 10 mM potassium phosphate buffer pH 7.0, 5.5 mM dextrose, 0.56 mM phenol red and 19 U/ml of HRPO) is added, together with the stimulant (200 nM PMA). The plates are incubated at 37°C for 2 hours and the reaction is stopped by adding 20 µl 1N NaOH per well. The absorbance is read at 610 nm. To
25 calculate the amount of H_2O_2 produced by the macrophages, a standard curve of a H_2O_2 solution of known molarity is performed for each experiment.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 24: Biological Effects of Agonists or Antagonists of the Invention

Astrocyte and Neuronal Assays

Agonists or antagonists of the invention, expressed in *Escherichia coli* and purified as described above, can be tested for activity in promoting the survival, neurite outgrowth, or phenotypic differentiation of cortical neuronal cells and for inducing the proliferation of glial fibrillary acidic protein immunopositive cells, astrocytes. The selection of cortical cells for the bioassay is based on the prevalent expression of FGF-1 and FGF-2 in cortical structures and on the previously reported enhancement of cortical neuronal survival resulting from FGF-2 treatment. A thymidine incorporation assay, for example, can be used to elucidate an agonist or antagonist of the invention's activity on these cells.

Moreover, previous reports describing the biological effects of FGF-2 (basic FGF) on cortical or hippocampal neurons *in vitro* have demonstrated increases in both neuron survival and neurite outgrowth (Walicke et al., "Fibroblast growth factor promotes survival of dissociated hippocampal neurons and enhances neurite extension." *Proc. Natl. Acad. Sci. USA* 83:3012-3016. (1986), assay herein incorporated by reference in its entirety). However, reports from experiments done on PC-12 cells suggest that these two responses are not necessarily synonymous and may depend on not only which FGF is being tested but also on which receptor(s) are expressed on the target cells. Using the primary cortical neuronal culture paradigm, the ability of an agonist or antagonist of the invention to induce neurite outgrowth can be compared to the response achieved with FGF-2 using, for example, a thymidine incorporation assay.

Fibroblast and endothelial cell assays

Human lung fibroblasts are obtained from Clonetics (San Diego, CA) and maintained in growth media from Clonetics. Dermal microvascular endothelial cells are obtained from Cell Applications (San Diego, CA). For proliferation assays, the human lung fibroblasts and dermal microvascular endothelial cells can be cultured at 5,000 cells/well in a 96-well plate for one day in growth medium. The cells are then incubated for one day in 0.1% BSA basal medium. After replacing the medium with fresh 0.1% BSA medium, the cells are incubated with the test proteins for 3 days. Alamar Blue (Alamar Biosciences, Sacramento, CA) is added to each well to a final concentration of 10%. The cells are incubated for 4 hr. Cell viability is measured by reading in a CytoFluor fluorescence reader. For the PGE₂ assays, the human lung fibroblasts are cultured at 5,000 cells/well in a 96-well plate for one day. After a medium change to 0.1% BSA basal medium, the cells are incubated with FGF-2 or agonists or antagonists of the invention with or without IL-1 α for 24 hours.

The supernatants are collected and assayed for PGE₂ by EIA kit (Cayman, Ann Arbor, MI). For the IL-6 assays, the human lung fibroblasts are cultured at 5,000 cells/well in a 96-well plate for one day. After a medium change to 0.1% BSA basal medium, the cells are incubated with FGF-2 or with or without agonists or antagonists of the invention IL-1 α for 24 hours. The supernatants are collected and
5 assayed for IL-6 by ELISA kit (Endogen, Cambridge, MA).

Human lung fibroblasts are cultured with FGF-2 or agonists or antagonists of the invention for 3 days in basal medium before the addition of Alamar Blue to assess effects on growth of the fibroblasts. FGF-2 should show a stimulation at 10 - 2500 ng/ml which can be used to compare stimulation with agonists or antagonists of the invention.

Parkinson Models.

The loss of motor function in Parkinson's disease is attributed to a deficiency of striatal dopamine resulting from the degeneration of the nigrostriatal dopaminergic projection neurons. An animal model for Parkinson's that has been extensively characterized involves the systemic
15 administration of 1-methyl-4 phenyl 1,2,3,6-tetrahydropyridine (MPTP). In the CNS, MPTP is taken-up by astrocytes and catabolized by monoamine oxidase B to 1-methyl-4-phenyl pyridine (MPP⁺) and released. Subsequently, MPP⁺ is actively accumulated in dopaminergic neurons by the high-affinity reuptake transporter for dopamine. MPP⁺ is then concentrated in mitochondria by the electrochemical gradient and selectively inhibits nicotinamide adenine disphosphate: ubiquinone oxidoreductionase
20 (complex I), thereby interfering with electron transport and eventually generating oxygen radicals.

It has been demonstrated in tissue culture paradigms that FGF-2 (basic FGF) has trophic activity towards nigral dopaminergic neurons (Ferrari et al., Dev. Biol. 1989). Recently, Dr. Unsicker's group has demonstrated that administering FGF-2 in gel foam implants in the striatum results in the near complete protection of nigral dopaminergic neurons from the toxicity associated with MPTP
25 exposure (Otto and Unsicker, J. Neuroscience, 1990).

Based on the data with FGF-2, agonists or antagonists of the invention can be evaluated to determine whether it has an action similar to that of FGF-2 in enhancing dopaminergic neuronal survival *in vitro* and it can also be tested *in vivo* for protection of dopaminergic neurons in the striatum from the damage associated with MPTP treatment. The potential effect of an agonist or antagonist of
30 the invention is first examined *in vitro* in a dopaminergic neuronal cell culture paradigm. The cultures are prepared by dissecting the midbrain floor plate from gestation day 14 Wistar rat embryos. The tissue is dissociated with trypsin and seeded at a density of 200,000 cells/cm² on polyorthinine-laminin coated glass coverslips. The cells are maintained in Dulbecco's Modified Eagle's medium and F12 medium containing hormonal supplements (N1). The cultures are fixed with paraformaldehyde after 8
35 days *in vitro* and are processed for tyrosine hydroxylase, a specific marker for dopaminergic neurons,

immunohistochemical staining. Dissociated cell cultures are prepared from embryonic rats. The culture medium is changed every third day and the factors are also added at that time.

Since the dopaminergic neurons are isolated from animals at gestation day 14, a developmental time which is past the stage when the dopaminergic precursor cells are proliferating, an increase in the number of tyrosine hydroxylase immunopositive neurons would represent an increase in the number of dopaminergic neurons surviving *in vitro*. Therefore, if an agonist or antagonist of the invention acts to prolong the survival of dopaminergic neurons, it would suggest that the agonist or antagonist may be involved in Parkinson's Disease.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 25: The Effect of Agonists or Antagonists of the Invention on the Growth of Vascular Endothelial Cells

On day 1, human umbilical vein endothelial cells (HUVEC) are seeded at $2-5 \times 10^4$ cells/35 mm dish density in M199 medium containing 4% fetal bovine serum (FBS), 16 units/ml heparin, and 50 units/ml endothelial cell growth supplements (ECGS, Biotechnology, Inc.). On day 2, the medium is replaced with M199 containing 10% FBS, 8 units/ml heparin. An agonist or antagonist of the invention, and positive controls, such as VEGF and basic FGF (bFGF) are added, at varying concentrations. On days 4 and 6, the medium is replaced. On day 8, cell number is determined with a Coulter Counter.

An increase in the number of HUVEC cells indicates that the compound of the invention may proliferate vascular endothelial cells, while a decrease in the number of HUVEC cells indicates that the compound of the invention inhibits vascular endothelial cells.

The studies described in this example tested activity of a polypeptide of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), agonists, and/or antagonists of the invention.

30

Example 26: Rat Corneal Wound Healing Model

This animal model shows the effect of an agonist or antagonist of the invention on neovascularization. The experimental protocol includes:

35 Making a 1-1.5 mm long incision from the center of cornea into the stromal layer.

Inserting a spatula below the lip of the incision facing the outer corner of the eye.

Making a pocket (its base is 1-1.5 mm from the edge of the eye).

Positioning a pellet, containing 50ng- 5ug of an agonist or antagonist of the invention, within the pocket.

Treatment with an agonist or antagonist of the invention can also be applied topically to the corneal wounds in a dosage range of 20mg - 500mg (daily treatment for five days).

- 5 The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

**Example 27: Diabetic Mouse and Glucocorticoid-Impaired
Wound Healing Models**

10

Diabetic db+/db+ Mouse Model.

- To demonstrate that an agonist or antagonist of the invention accelerates the healing process, the genetically diabetic mouse model of wound healing is used. The full thickness wound healing model in the db+/db+ mouse is a well characterized, clinically relevant and reproducible model of impaired wound healing. Healing of the diabetic wound is dependent on formation of granulation tissue and re-epithelialization rather than contraction (Gartner, M.H. *et al.*, *J. Surg. Res.* 52:389 (1992); Greenhalgh, D.G. *et al.*, *Am. J. Pathol.* 136:1235 (1990)).

- The diabetic animals have many of the characteristic features observed in Type II diabetes mellitus. Homozygous (db+/db+) mice are obese in comparison to their normal heterozygous (db+/+m) littermates. Mutant diabetic (db+/db+) mice have a single autosomal recessive mutation on chromosome 4 (db+) (Coleman *et al.* *Proc. Natl. Acad. Sci. USA* 77:283-293 (1982)). Animals show polyphagia, polydipsia and polyuria. Mutant diabetic mice (db+/db+) have elevated blood glucose, increased or normal insulin levels, and suppressed cell-mediated immunity (Mandel *et al.*, *J. Immunol.* 120:1375 (1978); Debray-Sachs, M. *et al.*, *Clin. Exp. Immunol.* 51(1):1-7 (1983); Leiter *et al.*, *Am. J. of Pathol.* 114:46-55 (1985)). Peripheral neuropathy, myocardial complications, and microvascular lesions, basement membrane thickening and glomerular filtration abnormalities have been described in these animals (Norido, F. *et al.*, *Exp. Neurol.* 83(2):221-232 (1984); Robertson *et al.*, *Diabetes* 29(1):60-67 (1980); Giacomelli *et al.*, *Lab Invest.* 40(4):460-473 (1979); Coleman, D.L., *Diabetes* 31 (Suppl):1-6 (1982)). These homozygous diabetic mice develop hyperglycemia that is resistant to insulin analogous to human type II diabetes (Mandel *et al.*, *J. Immunol.* 120:1375-1377 (1978)).

- The characteristics observed in these animals suggests that healing in this model may be similar to the healing observed in human diabetes (Greenhalgh, *et al.*, *Am. J. of Pathol.* 136:1235-1246 (1990)).

- 35 Genetically diabetic female C57BL/KsJ (db+/db+) mice and their non-diabetic (db+/+m) heterozygous littermates are used in this study (Jackson Laboratories). The animals are purchased at 6 weeks of age and are 8 weeks old at the beginning of the study. Animals are individually housed and

received food and water ad libitum. All manipulations are performed using aseptic techniques. The experiments are conducted according to the rules and guidelines of Human Genome Sciences, Inc. Institutional Animal Care and Use Committee and the Guidelines for the Care and Use of Laboratory Animals.

5 Wounding protocol is performed according to previously reported methods (Tsuboi, R. and Rifkin, D.B., *J. Exp. Med.* 172:245-251 (1990)). Briefly, on the day of wounding, animals are anesthetized with an intraperitoneal injection of Avertin (0.01 mg/mL), 2,2,2-tribromoethanol and 2-methyl-2-butanol dissolved in deionized water. The dorsal region of the animal is shaved and the skin washed with 70% ethanol solution and iodine. The surgical area is dried with sterile gauze prior to
10 wounding. An 8 mm full-thickness wound is then created using a Keyes tissue punch. Immediately following wounding, the surrounding skin is gently stretched to eliminate wound expansion. The wounds are left open for the duration of the experiment. Application of the treatment is given topically for 5 consecutive days commencing on the day of wounding. Prior to treatment, wounds are gently cleansed with sterile saline and gauze sponges.

15 Wounds are visually examined and photographed at a fixed distance at the day of surgery and at two day intervals thereafter. Wound closure is determined by daily measurement on days 1-5 and on day 8. Wounds are measured horizontally and vertically using a calibrated Jameson caliper. Wounds are considered healed if granulation tissue is no longer visible and the wound is covered by a continuous epithelium.

20 An agonist or antagonist of the invention is administered using at a range different doses, from 4mg to 500mg per wound per day for 8 days in vehicle. Vehicle control groups received 50mL of vehicle solution.

 Animals are euthanized on day 8 with an intraperitoneal injection of sodium pentobarbital (300mg/kg). The wounds and surrounding skin are then harvested for histology and
25 immunohistochemistry. Tissue specimens are placed in 10% neutral buffered formalin in tissue cassettes between biopsy sponges for further processing.

 Three groups of 10 animals each (5 diabetic and 5 non-diabetic controls) are evaluated: 1) Vehicle placebo control, 2) untreated group, and 3) treated group.

 Wound closure is analyzed by measuring the area in the vertical and horizontal axis and
30 obtaining the total square area of the wound. Contraction is then estimated by establishing the differences between the initial wound area (day 0) and that of post treatment (day 8). The wound area on day 1 is 64mm², the corresponding size of the dermal punch. Calculations are made using the following formula:

35 [Open area on day 8] - [Open area on day 1] / [Open area on day 1]

Specimens are fixed in 10% buffered formalin and paraffin embedded blocks are sectioned perpendicular to the wound surface (5mm) and cut using a Reichert-Jung microtome. Routine hematoxylin-eosin (H&E) staining is performed on cross-sections of bisected wounds. Histologic examination of the wounds are used to assess whether the healing process and the morphologic appearance of the repaired skin is altered by treatment with an agonist or antagonist of the invention. This assessment included verification of the presence of cell accumulation, inflammatory cells, capillaries, fibroblasts, re-epithelialization and epidermal maturity (Greenhalgh, D.G. *et al.*, *Am. J. Pathol.* 136:1235 (1990)). A calibrated lens micrometer is used by a blinded observer.

Tissue sections are also stained immunohistochemically with a polyclonal rabbit anti-human keratin antibody using ABC Elite detection system. Human skin is used as a positive tissue control while non-immune IgG is used as a negative control. Keratinocyte growth is determined by evaluating the extent of reepithelialization of the wound using a calibrated lens micrometer.

Proliferating cell nuclear antigen/cyclin (PCNA) in skin specimens is demonstrated by using anti-PCNA antibody (1:50) with an ABC Elite detection system. Human colon cancer served as a positive tissue control and human brain tissue is used as a negative tissue control. Each specimen included a section with omission of the primary antibody and substitution with non-immune mouse IgG. Ranking of these sections is based on the extent of proliferation on a scale of 0-8, the lower side of the scale reflecting slight proliferation to the higher side reflecting intense proliferation.

Experimental data are analyzed using an unpaired t test. A p value of < 0.05 is considered significant.

Steroid Impaired Rat Model

The inhibition of wound healing by steroids has been well documented in various *in vitro* and *in vivo* systems (Wahl, Glucocorticoids and Wound healing. In: Anti-Inflammatory Steroid Action: Basic and Clinical Aspects. 280-302 (1989); Wahl *et al.*, *J. Immunol.* 115: 476-481 (1975); Werb *et al.*, *J. Exp. Med.* 147:1684-1694 (1978)). Glucocorticoids retard wound healing by inhibiting angiogenesis, decreasing vascular permeability (Ebert *et al.*, *An. Intern. Med.* 37:701-705 (1952)), fibroblast proliferation, and collagen synthesis (Beck *et al.*, *Growth Factors.* 5: 295-304 (1991); Haynes *et al.*, *J. Clin. Invest.* 61: 703-797 (1978)) and producing a transient reduction of circulating monocytes (Haynes *et al.*, *J. Clin. Invest.* 61: 703-797 (1978); Wahl, "Glucocorticoids and wound healing", In: Antiinflammatory Steroid Action: Basic and Clinical Aspects, Academic Press, New York, pp. 280-302 (1989)). The systemic administration of steroids to impaired wound healing is a well establish phenomenon in rats (Beck *et al.*, *Growth Factors.* 5: 295-304 (1991); Haynes *et al.*, *J. Clin. Invest.* 61: 703-797 (1978); Wahl, "Glucocorticoids and wound healing", In: Antiinflammatory Steroid Action: Basic and Clinical Aspects, Academic Press, New York, pp. 280-302 (1989); Pierce *et al.*, *Proc. Natl. Acad. Sci. USA* 86: 2229-2233 (1989)).

To demonstrate that an agonist or antagonist of the invention can accelerate the healing process, the effects of multiple topical applications of the agonist or antagonist on full thickness excisional skin wounds in rats in which healing has been impaired by the systemic administration of methylprednisolone is assessed.

5 Young adult male Sprague Dawley rats weighing 250-300 g (Charles River Laboratories) are used in this example. The animals are purchased at 8 weeks of age and are 9 weeks old at the beginning of the study. The healing response of rats is impaired by the systemic administration of methylprednisolone (17mg/kg/rat intramuscularly) at the time of wounding. Animals are individually housed and received food and water *ad libitum*. All manipulations are performed using aseptic techniques. This study is conducted according to the rules and guidelines of Human Genome Sciences, Inc. Institutional Animal Care and Use Committee and the Guidelines for the Care and Use of Laboratory Animals.

10 The wounding protocol is followed according to section A, above. On the day of wounding, animals are anesthetized with an intramuscular injection of ketamine (50 mg/kg) and xylazine (5 mg/kg). The dorsal region of the animal is shaved and the skin washed with 70% ethanol and iodine solutions. The surgical area is dried with sterile gauze prior to wounding. An 8 mm full-thickness wound is created using a Keyes tissue punch. The wounds are left open for the duration of the experiment. Applications of the testing materials are given topically once a day for 7 consecutive days commencing on the day of wounding and subsequent to methylprednisolone administration. Prior to treatment, wounds are gently cleansed with sterile saline and gauze sponges.

20 Wounds are visually examined and photographed at a fixed distance at the day of wounding and at the end of treatment. Wound closure is determined by daily measurement on days 1-5 and on day 8. Wounds are measured horizontally and vertically using a calibrated Jameson caliper. Wounds are considered healed if granulation tissue is no longer visible and the wound is covered by a continuous epithelium.

25 The agonist or antagonist of the invention is administered using at a range different doses, from 4mg to 500mg per wound per day for 8 days in vehicle. Vehicle control groups received 50mL of vehicle solution.

30 Animals are euthanized on day 8 with an intraperitoneal injection of sodium pentobarbital (300mg/kg). The wounds and surrounding skin are then harvested for histology. Tissue specimens are placed in 10% neutral buffered formalin in tissue cassettes between biopsy sponges for further processing.

35 Three groups of 10 animals each (5 with methylprednisolone and 5 without glucocorticoid) are evaluated: 1) Untreated group 2) Vehicle placebo control 3) treated groups.

 Wound closure is analyzed by measuring the area in the vertical and horizontal axis and obtaining the total area of the wound. Closure is then estimated by establishing the differences between

the initial wound area (day 0) and that of post treatment (day 8). The wound area on day 1 is 64mm², the corresponding size of the dermal punch. Calculations are made using the following formula:

$$[\text{Open area on day 8}] - [\text{Open area on day 1}] / [\text{Open area on day 1}]$$

5

Specimens are fixed in 10% buffered formalin and paraffin embedded blocks are sectioned perpendicular to the wound surface (5mm) and cut using an Olympus microtome. Routine hematoxylin-eosin (H&E) staining is performed on cross-sections of bisected wounds. Histologic examination of the wounds allows assessment of whether the healing process and the morphologic appearance of the repaired skin is improved by treatment with an agonist or antagonist of the invention. A calibrated lens micrometer is used by a blinded observer to determine the distance of the wound gap.

Experimental data are analyzed using an unpaired t test. A p value of < 0.05 is considered significant.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 28: Lymphadema Animal Model

The purpose of this experimental approach is to create an appropriate and consistent lymphedema model for testing the therapeutic effects of an agonist or antagonist of the invention in lymphangiogenesis and re-establishment of the lymphatic circulatory system in the rat hind limb. Effectiveness is measured by swelling volume of the affected limb, quantification of the amount of lymphatic vasculature, total blood plasma protein, and histopathology. Acute lymphedema is observed for 7-10 days. Perhaps more importantly, the chronic progress of the edema is followed for up to 3-4 weeks.

Prior to beginning surgery, blood sample is drawn for protein concentration analysis. Male rats weighing approximately ~350g are dosed with Pentobarbital. Subsequently, the right legs are shaved from knee to hip. The shaved area is swabbed with gauze soaked in 70% EtOH. Blood is drawn for serum total protein testing. Circumference and volumetric measurements are made prior to injecting dye into paws after marking 2 measurement levels (0.5 cm above heel, at mid-pt of dorsal paw). The intradermal dorsum of both right and left paws are injected with 0.05 ml of 1% Evan's Blue. Circumference and volumetric measurements are then made following injection of dye into paws.

Using the knee joint as a landmark, a mid-leg inguinal incision is made circumferentially allowing the femoral vessels to be located. Forceps and hemostats are used to dissect and separate the skin flaps. After locating the femoral vessels, the lymphatic vessel that runs along side and underneath

the vessel(s) is located. The main lymphatic vessels in this area are then electrically coagulated or suture ligated.

Using a microscope, muscles in back of the leg (near the semitendinosus and adductors) are bluntly dissected. The popliteal lymph node is then located. The 2 proximal and 2 distal lymphatic vessels and distal blood supply of the popliteal node are then ligated by suturing. The popliteal lymph node, and any accompanying adipose tissue, is then removed by cutting connective tissues.

Care is taken to control any mild bleeding resulting from this procedure. After lymphatics are occluded, the skin flaps are sealed by using liquid skin (Vetbond) (AJ Buck). The separated skin edges are sealed to the underlying muscle tissue while leaving a gap of ~0.5 cm around the leg. Skin also may be anchored by suturing to underlying muscle when necessary.

To avoid infection, animals are housed individually with mesh (no bedding). Recovering animals are checked daily through the optimal edematous peak, which typically occurred by day 5-7. The plateau edematous peak are then observed. To evaluate the intensity of the lymphedema, the circumference and volumes of 2 designated places on each paw before operation and daily for 7 days are measured. The effect of plasma proteins on lymphedema is determined and whether protein analysis is a useful testing perimeter is also investigated. The weights of both control and edematous limbs are evaluated at 2 places. Analysis is performed in a blind manner.

Circumference Measurements: Under brief gas anesthetic to prevent limb movement, a cloth tape is used to measure limb circumference. Measurements are done at the ankle bone and dorsal paw by 2 different people and those 2 readings are averaged. Readings are taken from both control and edematous limbs.

Volumetric Measurements: On the day of surgery, animals are anesthetized with Pentobarbital and are tested prior to surgery. For daily volumetrics animals are under brief halothane anesthetic (rapid immobilization and quick recovery), and both legs are shaved and equally marked using waterproof marker on legs. Legs are first dipped in water, then dipped into instrument to each marked level then measured by Buxco edema software(Chen/Victor). Data is recorded by one person, while the other is dipping the limb to marked area.

Blood-plasma protein measurements: Blood is drawn, spun, and serum separated prior to surgery and then at conclusion for total protein and Ca^{2+} comparison.

Limb Weight Comparison: After drawing blood, the animal is prepared for tissue collection. The limbs are amputated using a quillitine, then both experimental and control legs are cut at the ligature and weighed. A second weighing is done as the tibio-cacaneal joint is disarticulated and the foot is weighed.

Histological Preparations: The transverse muscle located behind the knee (popliteal) area is dissected and arranged in a metal mold, filled with freezeGel, dipped into cold methylbutane, placed into labeled sample bags at - 80EC until sectioning. Upon sectioning, the muscle is observed under fluorescent microscopy for lymphatics..

Example 29: Suppression of TNF alpha-induced adhesion molecule expression by an Agonist or Antagonist of the Invention

Tumor necrosis factor alpha (TNF- α), a potent proinflammatory cytokine, is a stimulator of all three CAMs on endothelial cells and may be involved in a wide variety of inflammatory responses, often resulting in a pathological outcome.

To perform the experiment, human umbilical vein endothelial cell (HUVEC) cultures are obtained from pooled cord harvests and maintained in growth medium (EGM-2; Clonetics, San Diego, CA) supplemented with 10% FCS and 1% penicillin/streptomycin in a 37 degree C humidified incubator containing 5% CO₂. HUVECs are seeded in 96-well plates at concentrations of 1×10^4 cells/well in EGM medium at 37 degree C for 18-24 hrs or until confluent. The monolayers are subsequently washed 3 times with a serum-free solution of RPMI-1640 supplemented with 100 U/ml penicillin and 100 mg/ml streptomycin, and treated with a given cytokine and/or growth factor(s) for 24 h at 37 degree C. Following incubation, the cells are then evaluated for CAM expression.

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(integrin expression only). Plates are aspirated to remove medium and 100 μ l of 0.1% paraformaldehyde-PBS(with Ca^{++} and Mg^{++}) is added to each well. Plates are held at 4°C for 30 min.

Fixative is then removed from the wells and wells are washed 1X with PBS(+Ca,Mg)+0.5% BSA and drained. Do not allow the wells to dry. Add 10 μ l of diluted primary antibody to the test and control wells. Anti-ICAM-1-Biotin, Anti-VCAM-1-Biotin and Anti-E-selectin-Biotin are used at a concentration of 10 μ g/ml (1:10 dilution of 0.1 mg/ml stock antibody). Cells are incubated at 37°C for 30 min. in a humidified environment. Wells are washed X3 with PBS(+Ca,Mg)+0.5% BSA.

Then add 20 μ l of diluted ExtrAvidin-Alkaline Phosphatase (1:5,000 dilution) to each well and incubated at 37°C for 30 min. Wells are washed X3 with PBS(+Ca,Mg)+0.5% BSA. 1 tablet of p-Nitrophenol Phosphate pNPP is dissolved in 5 ml of glycine buffer (pH 10.4). 100 μ l of pNPP substrate in glycine buffer is added to each test well. Standard wells in triplicate are prepared from the working dilution of the ExtrAvidin-Alkaline Phosphatase in glycine buffer: 1:5,000 (10^0) > $10^{-0.5}$ > 10^{-1} > $10^{-1.5}$. 5 μ l of each dilution is added to triplicate wells and the resulting AP content in each well is 5.50 ng, 1.74 ng, 0.55 ng, 0.18 ng. 100 μ l of pNPP reagent must then be added to each of the standard wells. The plate must be incubated at 37°C for 4h. A volume of 50 μ l of 3M NaOH is added to all wells. The results are quantified on a plate reader at 405 nm. The background subtraction option is used on blank wells filled with glycine buffer only. The template is set up to indicate the concentration of AP-conjugate in each standard well [5.50 ng; 1.74 ng; 0.55 ng; 0.18 ng]. Results are indicated as amount of bound AP-conjugate in each sample.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 30: Production Of Polypeptide of the Invention For High-Throughput

25

Screening Assays

The following protocol produces a supernatant containing polypeptide of the present invention to be tested. This supernatant can then be used in the Screening Assays described in Examples 32-41.

30

First, dilute Poly-D-Lysine (644 587 Boehringer-Mannheim) stock solution (1mg/ml in PBS) 1:20 in PBS (w/o calcium or magnesium 17-516F Biowhittaker) for a working solution of 50ug/ml. Add 200 μ l of this solution to each well (24 well plates) and incubate at RT for 20 minutes. Be sure to distribute the solution over each well (note: a 12-channel pipetter may be used with tips on every other channel). Aspirate off the Poly-D-Lysine solution and rinse with 1ml PBS (Phosphate Buffered Saline). The PBS should remain in the well until just prior to plating the cells and plates may be poly-lysine coated in advance for up to two weeks.

35

Plate 293T cells (do not carry cells past P+20) at 2×10^5 cells/well in .5ml DMEM(Dulbecco's Modified Eagle Medium)(with 4.5 G/L glucose and L-glutamine (12-604F Biowhittaker))/10% heat inactivated FBS(14-503F Biowhittaker)/1x Penstrep(17-602E Biowhittaker). Let the cells grow overnight.

- 5 The next day, mix together in a sterile solution basin: 300 ul Lipofectamine (18324-012 Gibco/BRL) and 5ml Optimem I (31985070 Gibco/BRL)/96-well plate. With a small volume multi-channel pipetter, aliquot approximately 2ug of an expression vector containing a polynucleotide insert, produced by the methods described in Examples 8-10, into an appropriately labeled 96-well round bottom plate. With a multi-channel pipetter, add 50ul of the
- 10 Lipofectamine/Optimem I mixture to each well. Pipette up and down gently to mix. Incubate at RT 15-45 minutes. After about 20 minutes, use a multi-channel pipetter to add 150ul Optimem I to each well. As a control, one plate of vector DNA lacking an insert should be transfected with each set of transfections.

- Preferably, the transfection should be performed by tag-teaming the following tasks. By
- 15 tag-teaming, hands on time is cut in half, and the cells do not spend too much time on PBS. First, person A aspirates off the media from four 24-well plates of cells, and then person B rinses each well with .5-1ml PBS. Person A then aspirates off PBS rinse, and person B, using a 12-channel pipetter with tips on every other channel, adds the 200ul of DNA/Lipofectamine/Optimem I complex to the odd wells first, then to the even wells, to each row on the 24-well plates. Incubate
- 20 at 37 degree C for 6 hours.

- While cells are incubating, prepare appropriate media, either 1%BSA in DMEM with 1x penstrep, or HGS CHO-5 media (116.6 mg/L of CaCl₂ (anhyd); 0.00130 mg/L CuSO₄·5H₂O; 0.050 mg/L of Fe(NO₃)₃·9H₂O; 0.417 mg/L of FeSO₄·7H₂O; 311.80 mg/L of KCl; 28.64 mg/L of MgCl₂; 48.84 mg/L of MgSO₄; 6995.50 mg/L of NaCl; 2400.0 mg/L of NaHCO₃; 62.50 mg/L
- 25 of NaH₂PO₄·H₂O; 71.02 mg/L of Na₂HPO₄; .4320 mg/L of ZnSO₄·7H₂O; .002 mg/L of Arachidonic Acid ; 1.022 mg/L of Cholesterol; .070 mg/L of DL-alpha-Tocopherol-Acetate; 0.0520 mg/L of Linoleic Acid; 0.010 mg/L of Linolenic Acid; 0.010 mg/L of Myristic Acid; 0.010 mg/L of Oleic Acid; 0.010 mg/L of Palmitric Acid; 0.010 mg/L of Palmitic Acid; 100 mg/L of Pluronic F-68; 0.010 mg/L of Stearic Acid; 2.20 mg/L of Tween 80; 4551 mg/L of D-Glucose;
- 30 130.85 mg/ml of L- Alanine; 147.50 mg/ml of L-Arginine-HCL; 7.50 mg/ml of L-Asparagine-H₂O; 6.65 mg/ml of L-Aspartic Acid; 29.56 mg/ml of L-Cystine-2HCL-H₂O; 31.29 mg/ml of L-Cystine-2HCL; 7.35 mg/ml of L-Glutamic Acid; 365.0 mg/ml of L-Glutamine; 18.75 mg/ml of Glycine; 52.48 mg/ml of L-Histidine-HCL-H₂O; 106.97 mg/ml of L-Isoleucine; 111.45 mg/ml of L-Leucine; 163.75 mg/ml of L-Lysine HCL; 32.34 mg/ml of L-Methionine; 68.48 mg/ml of L-Phenylalanine; 40.0 mg/ml of L-Proline; 26.25 mg/ml of L-Serine; 101.05 mg/ml of L-Threonine;
- 35 19.22 mg/ml of L-Tryptophan; 91.79 mg/ml of L-Tyrosine-2Na-2H₂O; and 99.65 mg/ml of L-

Valine; 0.0035 mg/L of Biotin; 3.24 mg/L of D-Ca Pantothenate; 11.78 mg/L of Choline Chloride; 4.65 mg/L of Folic Acid; 15.60 mg/L of i-Inositol; 3.02 mg/L of Niacinamide; 3.00 mg/L of Pyridoxal HCL; 0.031 mg/L of Pyridoxine HCL; 0.319 mg/L of Riboflavin; 3.17 mg/L of Thiamine HCL; 0.365 mg/L of Thymidine; 0.680 mg/L of Vitamin B₁₂; 25 mM of HEPES

5 Buffer; 2.39 mg/L of Na Hypoxanthine; 0.105 mg/L of Lipoic Acid; 0.081 mg/L of Sodium Putrescine-2HCL; 55.0 mg/L of Sodium Pyruvate; 0.0067 mg/L of Sodium Selenite; 20uM of Ethanolamine; 0.122 mg/L of Ferric Citrate; 41.70 mg/L of Methyl-B-Cyclodextrin complexed with Linoleic Acid; 33.33 mg/L of Methyl-B-Cyclodextrin complexed with Oleic Acid; 10 mg/L of Methyl-B-Cyclodextrin complexed with Retinal Acetate. Adjust osmolarity to 327 mOsm) with

10 2mm glutamine and 1x penstrep. (BSA (81-068-3 Bayer) 100gm dissolved in 1L DMEM for a 10% BSA stock solution). Filter the media and collect 50 ul for endotoxin assay in 15ml polystyrene conical.

The transfection reaction is terminated, preferably by tag-teaming, at the end of the incubation period. Person A aspirates off the transfection media, while person B adds 1.5ml

15 appropriate media to each well. Incubate at 37 degree C for 45 or 72 hours depending on the media used: 1%BSA for 45 hours or CHO-5 for 72 hours.

On day four, using a 300ul multichannel pipetter, aliquot 600ul in one 1ml deep well plate and the remaining supernatant into a 2ml deep well. The supernatants from each well can then be used in the assays described in Examples 32-39.

20 It is specifically understood that when activity is obtained in any of the assays described below using a supernatant, the activity originates from either the polypeptide of the present invention directly (e.g., as a secreted protein) or by polypeptide of the present invention inducing expression of other proteins, which are then secreted into the supernatant. Thus, the invention further provides a method of identifying the protein in the supernatant characterized by an activity

25 in a particular assay.

Example 31: Construction of GAS Reporter Construct

One signal transduction pathway involved in the differentiation and proliferation of cells is called the Jaks-STATs pathway. Activated proteins in the Jaks-STATs pathway bind to gamma

30 activation site "GAS" elements or interferon-sensitive responsive element ("ISRE"), located in the promoter of many genes. The binding of a protein to these elements alter the expression of the associated gene.

GAS and ISRE elements are recognized by a class of transcription factors called Signal

35 Transducers and Activators of Transcription, or "STATs." There are six members of the STATs family. Stat1 and Stat3 are present in many cell types, as is Stat2 (as response to IFN-alpha is

widespread). Stat4 is more restricted and is not in many cell types though it has been found in T helper class I, cells after treatment with IL-12. Stat5 was originally called mammary growth factor, but has been found at higher concentrations in other cells including myeloid cells. It can be activated in tissue culture cells by many cytokines.

- 5 The STATs are activated to translocate from the cytoplasm to the nucleus upon tyrosine phosphorylation by a set of kinases known as the Janus Kinase ("Jaks") family. Jaks represent a distinct family of soluble tyrosine kinases and include Tyk2, Jak1, Jak2, and Jak3. These kinases display significant sequence similarity and are generally catalytically inactive in resting cells.

- The Jaks are activated by a wide range of receptors summarized in the Table below.
10 (Adapted from review by Schidler and Darnell, Ann. Rev. Biochem. 64:621-51 (1995)). A cytokine receptor family, capable of activating Jaks, is divided into two groups: (a) Class 1 includes receptors for IL-2, IL-3, IL-4, IL-6, IL-7, IL-9, IL-11, IL-12, IL-15, Epo, PRL, GH, G-CSF, GM-CSF, LIF, CNTF, and thrombopoietin; and (b) Class 2 includes IFN-a, IFN-g, and IL-10. The Class 1 receptors share a conserved cysteine motif (a set of four conserved cysteines and
15 one tryptophan) and a WSXWS motif (a membrane proximal region encoding Trp-Ser-Xaa-Trp-Ser (SEQ ID NO: 2)).

- Thus, on binding of a ligand to a receptor, Jaks are activated, which in turn activate STATs, which then translocate and bind to GAS elements. This entire process is encompassed in the Jaks-STATs signal transduction pathway. Therefore, activation of the Jaks-STATs pathway,
20 reflected by the binding of the GAS or the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. For example, growth factors and cytokines are known to activate the Jaks-STATs pathway (See Table below). Thus, by using GAS elements linked to reporter molecules, activators of the Jaks-STATs pathway can be identified.

		<u>JAKs</u>				<u>STATS GAS(elements) or ISRE</u>	
		<u>tyk2</u>	<u>Jak1</u>	<u>Jak2</u>	<u>Jak3</u>		
		<u>IFN family</u>					
5	IFN-a/B	+	+	-	-	1,2,3	ISRE
	IFN-g		+	+	-	1	GAS (IRF1>Lys6>IFP)
	IL-10	+	?	?	-	1,3	
		<u>gp130 family</u>					
10	IL-6 (Pleiotropic)	+	+	+	?	1,3	GAS (IRF1>Lys6>IFP)
	IL-11(Pleiotropic)	?	+	?	?	1,3	
	OnM(Pleiotropic)	?	+	+	?	1,3	
	LIF(Pleiotropic)	?	+	+	?	1,3	
	CNTF(Pleiotropic)	-/+	+	+	?	1,3	
15	G-CSF(Pleiotropic)	?	+	?	?	1,3	
	IL-12(Pleiotropic)	+	-	+	+	1,3	
		<u>g-C family</u>					
20	IL-2 (lymphocytes)	-	+	-	+	1,3,5	GAS
	IL-4 (lymph/myeloid)	-	+	-	+	6	GAS (IRF1 = IFP
	>>Ly6)(IgH)						
	IL-7 (lymphocytes)	-	+	-	+	5	GAS
	IL-9 (lymphocytes)	-	+	-	+	5	GAS
	IL-13 (lymphocyte)	-	+	?	?	6	GAS
25	IL-15	?	+	?	+	5	GAS
		<u>gp140 family</u>					
	IL-3 (myeloid)	-	-	+	-	5	GAS
	(IRF1>IFP>>Ly6)						
30	IL-5 (myeloid)	-	-	+	-	5	GAS
	GM-CSF (myeloid)	-	-	+	-	5	GAS
		<u>Growth hormone family</u>					
	GH	?	-	+	-	5	
35	PRL	?	+/-	+	-	1,3,5	
	EPO	?	-	+	-	5	GAS(B-
	CAS>IRF1=IFP>>Ly6)						
		<u>Receptor Tyrosine Kinases</u>					
40	EGF	?	+	+	-	1,3	GAS (IRF1)
	PDGF	?	+	+	-	1,3	
	CSF-1	?	+	+	-	1,3	GAS (not IRF1)

To construct a synthetic GAS containing promoter element, which is used in the Biological Assays described in Examples 32-33, a PCR based strategy is employed to generate a GAS-SV40 promoter sequence. The 5' primer contains four tandem copies of the GAS binding site found in the IRF1 promoter and previously demonstrated to bind STATs upon induction with a range of cytokines (Rothman et al., Immunity 1:457-468 (1994).), although other GAS or ISRE elements can be used instead. The 5' primer also contains 18bp of sequence complementary to the SV40 early promoter sequence and is flanked with an XhoI site. The sequence of the 5' primer is:

5':GCGCCTCGAGATTTCCTCGAAATCTAGATTTCCTCGAAATGATTTCCTCGAAATGATTTCCTCGAAATATCTGCCATCTCAATTAG:3' (SEQ ID NO: 3)

The downstream primer is complementary to the SV40 promoter and is flanked with a Hind III site: 5':GCGGCAAGCTTTTGGCAAAGCCTAGGC:3' (SEQ ID NO: 4)

PCR amplification is performed using the SV40 promoter template present in the B-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI/Hind III and subcloned into BLSK2-. (Stratagene.) Sequencing with forward and reverse primers confirms that the insert contains the following sequence:

5':CTCGAGATTTCCTCGAAATCTAGATTTCCTCGAAATGATTTCCTCGAAATGATTTCCTCGAAATATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCATCCCGCCCCTAACTCCGCCCAGTTCGCCCATCTCCGCCCATGGCTGACTAA
TTTTTTTTTATTTATGCAGAGGCCGAGGCCGCTCGGCCTCTGAGCTATTCCAGAAGTAG
TGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAGCTT:3' (SEQ ID NO: 5)

With this GAS promoter element linked to the SV40 promoter, a GAS:SEAP2 reporter construct is next engineered. Here, the reporter molecule is a secreted alkaline phosphatase, or "SEAP." Clearly, however, any reporter molecule can be instead of SEAP, in this or in any of the other Examples. Well known reporter molecules that can be used instead of SEAP include chloramphenicol acetyltransferase (CAT), luciferase, alkaline phosphatase, B-galactosidase, green fluorescent protein (GFP), or any protein detectable by an antibody.

The above sequence confirmed synthetic GAS-SV40 promoter element is subcloned into the pSEAP-Promoter vector obtained from Clontech using HindIII and XhoI, effectively replacing the SV40 promoter with the amplified GAS:SV40 promoter element, to create the GAS-SEAP vector. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

Thus, in order to generate mammalian stable cell lines expressing the GAS-SEAP reporter, the GAS-SEAP cassette is removed from the GAS-SEAP vector using SalI and NotI, and inserted into a backbone vector containing the neomycin resistance gene, such as pGFP-1 (Clontech), using these restriction sites in the multiple cloning site, to create the GAS-SEAP/Neo vector. Once this

vector is transfected into mammalian cells, this vector can then be used as a reporter molecule for GAS binding as described in Examples 32-33.

Other constructs can be made using the above description and replacing GAS with a different promoter sequence. For example, construction of reporter molecules containing EGR and NF-KB promoter sequences are described in Examples 34 and 35. However, many other promoters can be substituted using the protocols described in these Examples. For instance, SRE, IL-2, NFAT, or Osteocalcin promoters can be substituted, alone or in combination (e.g., GAS/NF-KB/EGR, GAS/NF-KB, IL-2/NFAT, or NF-KB/GAS). Similarly, other cell lines can be used to test reporter construct activity, such as HELA (epithelial), HUVEC (endothelial), Reh (B-cell), Saos-2 (osteoblast), HUVAC (aortic), or Cardiomyocyte.

Example 32: High-Throughput Screening Assay for T-cell Activity.

The following protocol is used to assess T-cell activity by identifying factors, and determining whether supernate containing a polypeptide of the invention proliferates and/or differentiates T-cells. T-cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 31. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The T-cell used in this assay is Jurkat T-cells (ATCC Accession No. TIB-152), although Molt-3 cells (ATCC Accession No. CRL-1552) and Molt-4 cells (ATCC Accession No. CRL-1582) cells can also be used.

Jurkat T-cells are lymphoblastic CD4⁺ Th1 helper cells. In order to generate stable cell lines, approximately 2 million Jurkat cells are transfected with the GAS-SEAP/neo vector using DMRIE-C (Life Technologies)(transfection procedure described below). The transfected cells are seeded to a density of approximately 20,000 cells per well and transfectants resistant to 1 mg/ml gentamicin selected. Resistant colonies are expanded and then tested for their response to increasing concentrations of interferon gamma. The dose response of a selected clone is demonstrated.

Specifically, the following protocol will yield sufficient cells for 75 wells containing 200 ul of cells. Thus, it is either scaled up, or performed in multiple to generate sufficient cells for multiple 96 well plates. Jurkat cells are maintained in RPMI + 10% serum with 1%Pen-Strep. Combine 2.5 mls of OPTI-MEM (Life Technologies) with 10 ug of plasmid DNA in a T25 flask. Add 2.5 ml OPTI-MEM containing 50 ul of DMRIE-C and incubate at room temperature for 15-45 mins.

During the incubation period, count cell concentration, spin down the required number of cells (10^7 per transfection), and resuspend in OPTI-MEM to a final concentration of 10^7 cells/ml.

Then add 1ml of 1×10^7 cells in OPTI-MEM to T25 flask and incubate at 37 degree C for 6 hrs. After the incubation, add 10 ml of RPMI + 15% serum.

The Jurkat:GAS-SEAP stable reporter lines are maintained in RPMI + 10% serum, 1 mg/ml Genticin, and 1% Pen-Strep. These cells are treated with supernatants containing polypeptide of the present invention or polypeptide of the present invention induced polypeptides as produced by the protocol described in Example 30.

On the day of treatment with the supernatant, the cells should be washed and resuspended in fresh RPMI + 10% serum to a density of 500,000 cells per ml. The exact number of cells required will depend on the number of supernatants being screened. For one 96 well plate, approximately 10 million cells (for 10 plates, 100 million cells) are required.

Transfer the cells to a triangular reservoir boat, in order to dispense the cells into a 96 well dish, using a 12 channel pipette. Using a 12 channel pipette, transfer 200 ul of cells into each well (therefore adding 100, 000 cells per well).

After all the plates have been seeded, 50 ul of the supernatants are transferred directly from the 96 well plate containing the supernatants into each well using a 12 channel pipette. In addition, a dose of exogenous interferon gamma (0.1, 1.0, 10 ng) is added to wells H9, H10, and H11 to serve as additional positive controls for the assay.

The 96 well dishes containing Jurkat cells treated with supernatants are placed in an incubator for 48 hrs (note: this time is variable between 48-72 hrs). 35 ul samples from each well are then transferred to an opaque 96 well plate using a 12 channel pipette. The opaque plates should be covered (using sellophene covers) and stored at -20 degree C until SEAP assays are performed according to Example 36. The plates containing the remaining treated cells are placed at 4 degree C and serve as a source of material for repeating the assay on a specific well if desired.

As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate Jurkat T cells. Over 30 fold induction is typically observed in the positive control wells.

The above protocol may be used in the generation of both transient, as well as, stable transfected cells, which would be apparent to those of skill in the art.

Example 33: High-Throughput Screening Assay Identifying Myeloid Activity

The following protocol is used to assess myeloid activity of polypeptide of the present invention by determining whether polypeptide of the present invention proliferates and/or differentiates myeloid cells. Myeloid cell activity is assessed using the GAS/SEAP/Neo construct

produced in Example 31. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The myeloid cell used in this assay is U937, a pre-monocyte cell line, although TF-1, HL60, or KG1 can be used.

To transiently transfect U937 cells with the GAS/SEAP/Neo construct produced in
5 Example 31, a DEAE-Dextran method (Kharbanda et. al., 1994, Cell Growth & Differentiation, 5:259-265) is used. First, harvest 2×10^7 U937 cells and wash with PBS. The U937 cells are usually grown in RPMI 1640 medium containing 10% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 mg/ml streptomycin.

Next, suspend the cells in 1 ml of 20 mM Tris-HCl (pH 7.4) buffer containing 0.5 mg/ml
10 DEAE-Dextran, 8 ug GAS-SEAP2 plasmid DNA, 140 mM NaCl, 5 mM KCl, 375 uM $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$, 1 mM MgCl_2 , and 675 uM CaCl_2 . Incubate at 37 degrees C for 45 min.

Wash the cells with RPMI 1640 medium containing 10% FBS and then resuspend in 10 ml complete medium and incubate at 37 degree C for 36 hr.

The GAS-SEAP/U937 stable cells are obtained by growing the cells in 400 ug/ml G418.
15 The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 400 ug/ml G418 for couple of passages.

These cells are tested by harvesting 1×10^8 cells (this is enough for ten 96-well plates assay) and wash with PBS. Suspend the cells in 200 ml above described growth medium, with a final density of 5×10^5 cells/ml. Plate 200 ul cells per well in the 96-well plate (or 1×10^5
20 cells/well).

Add 50 ul of the supernatant prepared by the protocol described in Example 30. Incubate at 37 degree C for 48 to 72 hr. As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate U937 cells. Over 30 fold induction is typically observed in the positive control wells. SEAP assay the supernatant according to the protocol described in Example 36.
25

Example 34: High-Throughput Screening Assay Identifying Neuronal Activity.

When cells undergo differentiation and proliferation, a group of genes are activated through many different signal transduction pathways. One of these genes, EGR1 (early growth
30 response gene 1), is induced in various tissues and cell types upon activation. The promoter of EGR1 is responsible for such induction. Using the EGR1 promoter linked to reporter molecules, activation of cells can be assessed by polypeptide of the present invention.

Particularly, the following protocol is used to assess neuronal activity in PC12 cell lines. PC12 cells (rat phenochromocytoma cells) are known to proliferate and/or differentiate by
35 activation with a number of mitogens, such as TPA (tetradecanoyl phorbol acetate), NGF (nerve

growth factor), and EGF (epidermal growth factor). The EGR1 gene expression is activated during this treatment. Thus, by stably transfecting PC12 cells with a construct containing an EGR promoter linked to SEAP reporter, activation of PC12 cells by polypeptide of the present invention can be assessed.

- 5 The EGR/SEAP reporter construct can be assembled by the following protocol. The EGR-1 promoter sequence (-633 to +1)(Sakamoto K et al., Oncogene 6:867-871 (1991)) can be PCR amplified from human genomic DNA using the following primers:

5' GCGCTCGAGGGATGACAGCGATAGAACCCCGG-3' (SEQ ID NO: 6)

5' GCGAAGCTTCGCGACTCCCCGGATCCGCCTC-3' (SEQ ID NO: 7)

- 10 Using the GAS:SEAP/Neo vector produced in Example 31, EGR1 amplified product can then be inserted into this vector. Linearize the GAS:SEAP/Neo vector using restriction enzymes XhoI/HindIII, removing the GAS/SV40 stuffer. Restrict the EGR1 amplified product with these same enzymes. Ligate the vector and the EGR1 promoter.

- 15 To prepare 96 well-plates for cell culture, two mls of a coating solution (1:30 dilution of collagen type I (Upstate Biotech Inc. Cat#08-115) in 30% ethanol (filter sterilized)) is added per one 10 cm plate or 50 ml per well of the 96-well plate, and allowed to air dry for 2 hr.

- 20 PC12 cells are routinely grown in RPMI-1640 medium (Bio Whittaker) containing 10% horse serum (JRH BIOSCIENCES, Cat. # 12449-78P), 5% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 ug/ml streptomycin on a precoated 10 cm tissue culture dish. One to four split is done every three to four days. Cells are removed from the plates by scraping and resuspended with pipetting up and down for more than 15 times.

- 25 Transfect the EGR/SEAP/Neo construct into PC12 using the Lipofectamine protocol described in Example 30. EGR-SEAP/PC12 stable cells are obtained by growing the cells in 300 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 300 ug/ml G418 for couple of passages.

- To assay for neuronal activity, a 10 cm plate with cells around 70 to 80% confluent is screened by removing the old medium. Wash the cells once with PBS (Phosphate buffered saline). Then starve the cells in low serum medium (RPMI-1640 containing 1% horse serum and 0.5% FBS with antibiotics) overnight.

- 30 The next morning, remove the medium and wash the cells with PBS. Scrape off the cells from the plate, suspend the cells well in 2 ml low serum medium. Count the cell number and add more low serum medium to reach final cell density as 5×10^5 cells/ml.

- 35 Add 200 ul of the cell suspension to each well of 96-well plate (equivalent to 1×10^5 cells/well). Add 50 ul supernatant produced by Example 30, 37 degree C for 48 to 72 hr. As a positive control, a growth factor known to activate PC12 cells through EGR can be used, such as

50 ng/ul of Neuronal Growth Factor (NGF). Over fifty-fold induction of SEAP is typically seen in the positive control wells. SEAP assay the supernatant according to Example 36.

Example 35: High-Throughput Screening Assay for T-cell Activity

5

NF-KB (Nuclear Factor KB) is a transcription factor activated by a wide variety of agents including the inflammatory cytokines IL-1 and TNF, CD30 and CD40, lymphotoxin-alpha and lymphotoxin-beta, by exposure to LPS or thrombin, and by expression of certain viral gene products. As a transcription factor, NF-KB regulates the expression of genes involved in immune cell activation, control of apoptosis (NF- KB appears to shield cells from apoptosis), B and T-cell development, anti-viral and antimicrobial responses, and multiple stress responses.

In non-stimulated conditions, NF- KB is retained in the cytoplasm with I-KB (Inhibitor KB). However, upon stimulation, I- KB is phosphorylated and degraded, causing NF- KB to shuttle to the nucleus, thereby activating transcription of target genes. Target genes activated by NF- KB include IL-2, IL-6, GM-CSF, ICAM-1 and class 1 MHC.

Due to its central role and ability to respond to a range of stimuli, reporter constructs utilizing the NF-KB promoter element are used to screen the supernatants produced in Example 30. Activators or inhibitors of NF-KB would be useful in detecting, preventing, diagnosing, prognosticating, treating, and/or ameliorating diseases. For example, inhibitors of NF-KB could be used to treat those diseases related to the acute or chronic activation of NF-KB, such as rheumatoid arthritis.

To construct a vector containing the NF-KB promoter element, a PCR based strategy is employed. The upstream primer contains four tandem copies of the NF-KB binding site (GGGGACTTTCCC) (SEQ ID NO: 8), 18 bp of sequence complementary to the 5' end of the SV40 early promoter sequence, and is flanked with an XhoI site:

5':GCGGCCTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGACTTT
CCATCCTGCCATCTCAATTAG:3' (SEQ ID NO: 9)

The downstream primer is complementary to the 3' end of the SV40 promoter and is flanked with a Hind III site:

5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO: 4)

PCR amplification is performed using the SV40 promoter template present in the pB-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI and Hind III and subcloned into BLSK2-. (Stratagene) Sequencing with the T7 and T3 primers confirms the insert contains the following sequence:

5':CTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGACTTTCCATC
 TGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGCCCCT
 AACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTATTTATG
 CAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTT
 5 TGGAGGCCTAGGCTTTTGCAAAAAGCTT:3' (SEQ ID NO: 10)

Next, replace the SV40 minimal promoter element present in the pSEAP2-promoter plasmid (Clontech) with this NF-KB/SV40 fragment using XhoI and HindIII. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

10 In order to generate stable mammalian cell lines, the NF-KB/SV40/SEAP cassette is removed from the above NF-KB/SEAP vector using restriction enzymes SalI and NotI, and inserted into a vector containing neomycin resistance. Particularly, the NF-KB/SV40/SEAP cassette was inserted into pGFP-1 (Clontech), replacing the GFP gene, after restricting pGFP-1 with SalI and NotI.

15 Once NF-KB/SV40/SEAP/Neo vector is created, stable Jurkat T-cells are created and maintained according to the protocol described in Example 32. Similarly, the method for assaying supernatants with these stable Jurkat T-cells is also described in Example 32. As a positive control, exogenous TNF alpha (0.1, 1, 10 ng) is added to wells H9, H10, and H11, with a 5-10 fold activation typically observed.

20

Example 36: Assay for SEAP Activity

As a reporter molecule for the assays described in Examples 32-35, SEAP activity is assayed using the Tropix Phospho-light Kit (Cat. BP-400) according to the following general
 25 procedure. The Tropix Phospho-light Kit supplies the Dilution, Assay, and Reaction Buffers used below.

Prime a dispenser with the 2.5x Dilution Buffer and dispense 15 ul of 2.5x dilution buffer into Optiplates containing 35 ul of a supernatant. Seal the plates with a plastic sealer and incubate at 65 degree C for 30 min. Separate the Optiplates to avoid uneven heating.

30 Cool the samples to room temperature for 15 minutes. Empty the dispenser and prime with the Assay Buffer. Add 50 ml Assay Buffer and incubate at room temperature 5 min. Empty the dispenser and prime with the Reaction Buffer (see the Table below). Add 50 ul Reaction Buffer and incubate at room temperature for 20 minutes. Since the intensity of the chemiluminescent signal is time dependent, and it takes about 10 minutes to read 5 plates on a
 35 luminometer, thus one should treat 5 plates at each time and start the second set 10 minutes later.

Read the relative light unit in the luminometer. Set H12 as blank, and print the results.

An increase in chemiluminescence indicates reporter activity.

Reaction Buffer Formulation:

# of plates	Rxn buffer diluent (ml)	CSPD (ml)
10	60	3
11	65	3.25
12	70	3.5
13	75	3.75
14	80	4
15	85	4.25
16	90	4.5
17	95	4.75
18	100	5
19	105	5.25
20	110	5.5
21	115	5.75
22	120	6
23	125	6.25
24	130	6.5
25	135	6.75
26	140	7
27	145	7.25
28	150	7.5
29	155	7.75
30	160	8
31	165	8.25
32	170	8.5
33	175	8.75
34	180	9
35	185	9.25
36	190	9.5
37	195	9.75
38	200	10
39	205	10.25
40	210	10.5
41	215	10.75
42	220	11
43	225	11.25
44	230	11.5
45	235	11.75
46	240	12
47	245	12.25
48	250	12.5
49	255	12.75
50	260	13

Example 37: High-Throughput Screening Assay Identifying Changes in Small Molecule Concentration and Membrane Permeability

Binding of a ligand to a receptor is known to alter intracellular levels of small molecules, such as calcium, potassium, sodium, and pH, as well as alter membrane potential. These alterations can be measured in an assay to identify supernatants which bind to receptors of a particular cell. Although the following protocol describes an assay for calcium, this protocol can easily be modified to detect changes in potassium, sodium, pH, membrane potential, or any other small molecule which is detectable by a fluorescent probe.

The following assay uses Fluorometric Imaging Plate Reader ("FLIPR") to measure changes in fluorescent molecules (Molecular Probes) that bind small molecules. Clearly, any fluorescent molecule detecting a small molecule can be used instead of the calcium fluorescent molecule, fluo-4 (Molecular Probes, Inc.; catalog no. F-14202), used here.

For adherent cells, seed the cells at 10,000 -20,000 cells/well in a Co-star black 96-well plate with clear bottom. The plate is incubated in a CO₂ incubator for 20 hours. The adherent cells are washed two times in Biotek washer with 200 ul of HBSS (Hank's Balanced Salt Solution) leaving 100 ul of buffer after the final wash.

A stock solution of 1 mg/ml fluo-4 is made in 10% pluronic acid DMSO. To load the cells with fluo-4, 50 ul of 12 ug/ml fluo-4 is added to each well. The plate is incubated at 37 degrees C in a CO₂ incubator for 60 min. The plate is washed four times in the Biotek washer with HBSS leaving 100 ul of buffer.

For non-adherent cells, the cells are spun down from culture media. Cells are re-suspended to 2-5x10⁶ cells/ml with HBSS in a 50-ml conical tube. 4 ul of 1 mg/ml fluo-4 solution in 10% pluronic acid DMSO is added to each ml of cell suspension. The tube is then placed in a 37 degrees C water bath for 30-60 min. The cells are washed twice with HBSS, resuspended to 1x10⁶ cells/ml, and dispensed into a microplate, 100 ul/well. The plate is centrifuged at 1000 rpm for 5 min. The plate is then washed once in Denley Cell Wash with 200 ul, followed by an aspiration step to 100 ul final volume.

For a non-cell based assay, each well contains a fluorescent molecule, such as fluo-4. The supernatant is added to the well, and a change in fluorescence is detected.

To measure the fluorescence of intracellular calcium, the FLIPR is set for the following parameters: (1) System gain is 300-800 mW; (2) Exposure time is 0.4 second; (3) Camera F/stop is F/2; (4) Excitation is 488 nm; (5) Emission is 530 nm; and (6) Sample addition is 50 ul. Increased emission at 530 nm indicates an extracellular signaling event caused by the a molecule,

either polypeptide of the present invention or a molecule induced by polypeptide of the present invention, which has resulted in an increase in the intracellular Ca^{++} concentration.

Example 38: High-Throughput Screening Assay Identifying Tyrosine Kinase Activity

5

The Protein Tyrosine Kinases (PTK) represent a diverse group of transmembrane and cytoplasmic kinases. Within the Receptor Protein Tyrosine Kinase RPTK) group are receptors for a range of mitogenic and metabolic growth factors including the PDGF, FGF, EGF, NGF, HGF and Insulin receptor subfamilies. In addition there are a large family of RPTKs for which the
10 corresponding ligand is unknown. Ligands for RPTKs include mainly secreted small proteins, but also membrane-bound and extracellular matrix proteins.

Activation of RPTK by ligands involves ligand-mediated receptor dimerization, resulting in transphosphorylation of the receptor subunits and activation of the cytoplasmic tyrosine kinases. The cytoplasmic tyrosine kinases include receptor associated tyrosine kinases of the src-family
15 (e.g., src, yes, lck, lyn, fyn) and non-receptor linked and cytosolic protein tyrosine kinases, such as the Jak family, members of which mediate signal transduction triggered by the cytokine superfamily of receptors (e.g., the Interleukins, Interferons, GM-CSF, and Leptin).

Because of the wide range of known factors capable of stimulating tyrosine kinase activity, identifying whether polypeptide of the present invention or a molecule induced by
20 polypeptide of the present invention is capable of activating tyrosine kinase signal transduction pathways is of interest. Therefore, the following protocol is designed to identify such molecules capable of activating the tyrosine kinase signal transduction pathways.

Seed target cells (e.g., primary keratinocytes) at a density of approximately 25,000 cells per well in a 96 well Loprodyne Silent Screen Plates purchased from Nalge Nunc (Naperville, IL).
25 The plates are sterilized with two 30 minute rinses with 100% ethanol, rinsed with water and dried overnight. Some plates are coated for 2 hr with 100 ml of cell culture grade type I collagen (50 mg/ml), gelatin (2%) or polylysine (50 mg/ml), all of which can be purchased from Sigma Chemicals (St. Louis, MO) or 10% Matrigel purchased from Becton Dickinson (Bedford, MA), or calf serum, rinsed with PBS and stored at 4 degree C. Cell growth on these plates is assayed by
30 seeding 5,000 cells/well in growth medium and indirect quantitation of cell number through use of alamarBlue as described by the manufacturer Alamar Biosciences, Inc. (Sacramento, CA) after 48 hr. Falcon plate covers #3071 from Becton Dickinson (Bedford, MA) are used to cover the Loprodyne Silent Screen Plates. Falcon Microtest III cell culture plates can also be used in some proliferation experiments.

To prepare extracts, A431 cells are seeded onto the nylon membranes of Loprodyne plates (20,000/200ml/well) and cultured overnight in complete medium. Cells are quiesced by incubation in serum-free basal medium for 24 hr. After 5-20 minutes treatment with EGF (60ng/ml) or 50 ul of the supernatant produced in Example 30, the medium was removed and 100
5 ml of extraction buffer ((20 mM HEPES pH 7.5, 0.15 M NaCl, 1% Triton X-100, 0.1% SDS, 2 mM Na₃VO₄, 2 mM Na₄P₂O₇ and a cocktail of protease inhibitors (# 1836170) obtained from Boehringer Mannheim (Indianapolis, IN)) is added to each well and the plate is shaken on a rotating shaker for 5 minutes at 4°C. The plate is then placed in a vacuum transfer manifold and the extract filtered through the 0.45 mm membrane bottoms of each well using house vacuum.
10 Extracts are collected in a 96-well catch/assay plate in the bottom of the vacuum manifold and immediately placed on ice. To obtain extracts clarified by centrifugation, the content of each well, after detergent solubilization for 5 minutes, is removed and centrifuged for 15 minutes at 4 degree C at 16,000 x g.

Test the filtered extracts for levels of tyrosine kinase activity. Although many methods of
15 detecting tyrosine kinase activity are known, one method is described here.

Generally, the tyrosine kinase activity of a supernatant is evaluated by determining its ability to phosphorylate a tyrosine residue on a specific substrate (a biotinylated peptide). Biotinylated peptides that can be used for this purpose include PSK1 (corresponding to amino acids 6-20 of the cell division kinase cdc2-p34) and PSK2 (corresponding to amino acids 1-17 of
20 gastrin). Both peptides are substrates for a range of tyrosine kinases and are available from Boehringer Mannheim.

The tyrosine kinase reaction is set up by adding the following components in order. First, add 10ul of 5uM Biotinylated Peptide, then 10ul ATP/Mg₂₊ (5mM ATP/50mM MgCl₂), then 10ul of 5x Assay Buffer (40mM imidazole hydrochloride, pH7.3, 40 mM beta-glycerophosphate,
25 1mM EGTA, 100mM MgCl₂, 5 mM MnCl₂, 0.5 mg/ml BSA), then 5ul of Sodium Vanadate(1mM), and then 5ul of water. Mix the components gently and preincubate the reaction mix at 30 degree C for 2 min. Initiate the reaction by adding 10ul of the control enzyme or the filtered supernatant.

The tyrosine kinase assay reaction is then terminated by adding 10 ul of 120mM EDTA
30 and place the reactions on ice.

Tyrosine kinase activity is determined by transferring 50 ul aliquot of reaction mixture to a microtiter plate (MTP) module and incubating at 37 degree C for 20 min. This allows the streptavidin coated 96 well plate to associate with the biotinylated peptide. Wash the MTP module with 300ul/well of PBS four times. Next add 75 ul of anti-phosphotyrosine antibody conjugated to

horse radish peroxidase(anti-P-Tyr-POD(0.5u/ml)) to each well and incubate at 37 degree C for one hour. Wash the well as above.

Next add 100ul of peroxidase substrate solution (Boehringer Mannheim) and incubate at room temperature for at least 5 mins (up to 30 min). Measure the absorbance of the sample at 405 nm by using ELISA reader. The level of bound peroxidase activity is quantitated using an ELISA reader and reflects the level of tyrosine kinase activity.

Example 39: High-Throughput Screening Assay Identifying Phosphorylation Activity

As a potential alternative and/or complement to the assay of protein tyrosine kinase activity described in Example 38, an assay which detects activation (phosphorylation) of major intracellular signal transduction intermediates can also be used. For example, as described below one particular assay can detect tyrosine phosphorylation of the Erk-1 and Erk-2 kinases. However, phosphorylation of other molecules, such as Raf, JNK, p38 MAP, Map kinase kinase (MEK), MEK kinase, Src, Muscle specific kinase (MuSK), IRAK, Tec, and Janus, as well as any other phosphoserine, phosphotyrosine, or phosphothreonine molecule, can be detected by substituting these molecules for Erk-1 or Erk-2 in the following assay.

Specifically, assay plates are made by coating the wells of a 96-well ELISA plate with 0.1ml of protein G (1ug/ml) for 2 hr at room temp, (RT). The plates are then rinsed with PBS and blocked with 3% BSA/PBS for 1 hr at RT. The protein G plates are then treated with 2 commercial monoclonal antibodies (100ng/well) against Erk-1 and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this step can easily be modified by substituting a monoclonal antibody detecting any of the above described molecules.) After 3-5 rinses with PBS, the plates are stored at 4 degree C until use.

A431 cells are seeded at 20,000/well in a 96-well Loprodyne filterplate and cultured overnight in growth medium. The cells are then starved for 48 hr in basal medium (DMEM) and then treated with EGF (6ng/well) or 50 ul of the supernatants obtained in Example 30 for 5-20 minutes. The cells are then solubilized and extracts filtered directly into the assay plate.

After incubation with the extract for 1 hr at RT, the wells are again rinsed. As a positive control, a commercial preparation of MAP kinase (10ng/well) is used in place of A431 extract. Plates are then treated with a commercial polyclonal (rabbit) antibody (1ug/ml) which specifically recognizes the phosphorylated epitope of the Erk-1 and Erk-2 kinases (1 hr at RT). This antibody is biotinylated by standard procedures. The bound polyclonal antibody is then quantitated by successive incubations with Europium-streptavidin and Europium fluorescence enhancing reagent in the Wallac DELFIA instrument (time-resolved fluorescence). An increased fluorescent signal

over background indicates a phosphorylation by polypeptide of the present invention or a molecule induced by polypeptide of the present invention.

Example 40: Assay for the Stimulation of Bone Marrow CD34+ Cell Proliferation

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This assay is based on the ability of human CD34+ to proliferate in the presence of hematopoietic growth factors and evaluates the ability of isolated polypeptides expressed in mammalian cells to stimulate proliferation of CD34+ cells.

10 It has been previously shown that most mature precursors will respond to only a single signal. More immature precursors require at least two signals to respond. Therefore, to test the effect of polypeptides on hematopoietic activity of a wide range of progenitor cells, the assay contains a given polypeptide in the presence or absence of other hematopoietic growth factors. Isolated cells are cultured for 5 days in the presence of Stem Cell Factor (SCF) in combination with tested sample. SCF alone has a very limited effect on the proliferation of bone marrow (BM) cells, acting in such conditions only as a "survival" factor. However, combined with any factor exhibiting stimulatory effect on these cells (e.g., IL-3), SCF will cause a synergistic effect. Therefore, if the tested polypeptide has a stimulatory effect on hematopoietic progenitors, such activity can be easily detected. Since normal BM cells have a low level of cycling cells, it is likely that any inhibitory effect of a given polypeptide, or agonists or antagonists thereof, might not be detected. Accordingly, assays for an inhibitory effect on progenitors is preferably tested in cells that are first subjected to *in vitro* stimulation with SCF+IL-3, and then contacted with the compound that is being evaluated for inhibition of such induced proliferation.

25 Briefly, CD34+ cells are isolated using methods known in the art. The cells are thawed and resuspended in medium (QBSF 60 serum-free medium with 1% L-glutamine (500ml) Quality Biological, Inc., Gaithersburg, MD Cat# 160-204-101). After several gentle centrifugation steps at 200 x g, cells are allowed to rest for one hour. The cell count is adjusted to 2.5×10^5 cells/ml. During this time, 100 μ l of sterile water is added to the peripheral wells of a 96-well plate. The cytokines that can be tested with a given polypeptide in this assay is rhSCF (R&D Systems, Minneapolis, MN, Cat# 255-SC) at 50 ng/ml alone and in combination with rhSCF and rhIL-3 (R&D Systems, Minneapolis, MN, Cat# 203-ML) at 30 ng/ml. After one hour, 10 μ l of prepared cytokines, 50 μ l of the supernatants prepared in Example 30 (supernatants at 1:2 dilution = 50 μ l) and 20 μ l of diluted cells are added to the media which is already present in the wells to allow for a final total volume of 100 μ l. The plates are then placed in a 37°C/5% CO₂ incubator for five days.

35 Eighteen hours before the assay is harvested, 0.5 μ Ci/well of [3H] Thymidine is added in a 10 μ l volume to each well to determine the proliferation rate. The experiment is terminated by

harvesting the cells from each 96-well plate to a filtermat using the Tomtec Harvester 96. After harvesting, the filtermats are dried, trimmed and placed into OmniFilter assemblies consisting of one OmniFilter plate and one OmniFilter Tray. 60 μ l Microscint is added to each well and the plate sealed with TopSeal-A press-on sealing film. A bar code 15 sticker is affixed to the first plate for counting. The sealed plates are then loaded and the level of radioactivity determined via the Packard Top Count and the printed data collected for analysis. The level of radioactivity reflects the amount of cell proliferation.

The studies described in this example test the activity of a given polypeptide to stimulate bone marrow CD34+ cell proliferation. One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof. As a nonlimiting example, potential antagonists tested in this assay would be expected to inhibit cell proliferation in the presence of cytokines and/or to increase the inhibition of cell proliferation in the presence of cytokines and a given polypeptide. In contrast, potential agonists tested in this assay would be expected to enhance cell proliferation and/or to decrease the inhibition of cell proliferation in the presence of cytokines and a given polypeptide.

The ability of a gene to stimulate the proliferation of bone marrow CD34+ cells indicates that polynucleotides and polypeptides corresponding to the gene are useful for the detection, prevention, diagnosis, prognostication, treatment, and/or amelioration of disorders affecting the immune system and hematopoiesis. Representative uses are described in the "Immune Activity" and "Infectious Disease" sections above, and elsewhere herein.

Example 41: Assay for Extracellular Matrix Enhanced Cell Response (EMECCR)

The objective of the Extracellular Matrix Enhanced Cell Response (EMECCR) assay is to identify gene products (e.g., isolated polypeptides) that act on the hematopoietic stem cells in the context of the extracellular matrix (ECM) induced signal.

Cells respond to the regulatory factors in the context of signal(s) received from the surrounding microenvironment. For example, fibroblasts, and endothelial and epithelial stem cells fail to replicate in the absence of signals from the ECM. Hematopoietic stem cells can undergo self-renewal in the bone marrow, but not in *in vitro* suspension culture. The ability of stem cells to undergo self-renewal *in vitro* is dependent upon their interaction with the stromal cells and the ECM protein fibronectin (fn). Adhesion of cells to fn is mediated by the $\alpha_5\beta_1$ and $\alpha_4\beta_1$ integrin receptors, which are expressed by human and mouse hematopoietic stem cells. The factor(s) which integrate with the ECM environment and are responsible for stimulating stem cell self-

renewal have not yet been identified. Discovery of such factors should be of great interest in gene therapy and bone marrow transplant applications

Briefly, polystyrene, non tissue culture treated, 96-well plates are coated with fn fragment at a coating concentration of $0.2 \mu\text{g}/\text{cm}^2$. Mouse bone marrow cells are plated (1,000 cells/well)
5 in 0.2 ml of serum-free medium. Cells cultured in the presence of IL-3 (5 ng/ml) + SCF (50 ng/ml) would serve as the positive control, conditions under which little self-renewal but pronounced differentiation of the stem cells is to be expected. Gene products of the invention (e.g., including, but not limited to, polynucleotides and polypeptides of the present invention, and supernatants produced in Example 30), are tested with appropriate negative controls in the
10 presence and absence of SCF(5.0 ng/ml), where test factor supernatants represent 10% of the total assay volume. The plated cells are then allowed to grow by incubating in a low oxygen environment (5% CO_2 , 7% O_2 , and 88% N_2) tissue culture incubator for 7 days. The number of proliferating cells within the wells is then quantitated by measuring thymidine incorporation into cellular DNA. Verification of the positive hits in the assay will require phenotypic
15 characterization of the cells, which can be accomplished by scaling up of the culture system and using appropriate antibody reagents against cell surface antigens and FACScan.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof.

20 If a particular polypeptide of the present invention is found to be a stimulator of hematopoietic progenitors, polynucleotides and polypeptides corresponding to the gene encoding said polypeptide may be useful for the detection, prevention, diagnosis, prognostication, treatment, and/or amelioration of disorders affecting the immune system and hematopoiesis. Representative uses are described in the "Immune Activity" and "Infectious Disease" sections above, and
25 elsewhere herein. The gene product may also be useful in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

Additionally, the polynucleotides and/or polypeptides of the gene of interest and/or agonists and/or antagonists thereof, may also be employed to inhibit the proliferation and
30 differentiation of hematopoietic cells and therefore may be employed to protect bone marrow stem cells from chemotherapeutic agents during chemotherapy. This antiproliferative effect may allow administration of higher doses of chemotherapeutic agents and, therefore, more effective chemotherapeutic treatment.

Moreover, polynucleotides and polypeptides corresponding to the gene of interest may
35 also be useful for the detection, prevention, diagnosis, prognostication, treat, and/or amelioration

of hematopoietic related disorders such as, for example, anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex-vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia.

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Example 42: Human Dermal Fibroblast and Aortic Smooth Muscle Cell Proliferation

The polypeptide of interest is added to cultures of normal human dermal fibroblasts (NHDF) and human aortic smooth muscle cells (AoSMC) and two co-assays are performed with
10 each sample. The first assay examines the effect of the polypeptide of interest on the proliferation of normal human dermal fibroblasts (NHDF) or aortic smooth muscle cells (AoSMC). Aberrant growth of fibroblasts or smooth muscle cells is a part of several pathological processes, including fibrosis, and restenosis. The second assay examines IL6 production by both NHDF and SMC. IL6
15 production is an indication of functional activation. Activated cells will have increased production of a number of cytokines and other factors, which can result in a proinflammatory or immunomodulatory outcome. Assays are run with and without co-TNF α stimulation, in order to check for costimulatory or inhibitory activity.

Briefly, on day 1, 96-well black plates are set up with 1000 cells/well (NHDF) or 2000 cells/well (AoSMC) in 100 μ l culture media. NHDF culture media contains: Clonetics FB basal
20 media, 1mg/ml hFGF, 5mg/ml insulin, 50mg/ml gentamycin, 2%FBS, while AoSMC culture media contains Clonetics SM basal media, 0.5 μ g/ml hEGF, 5mg/ml insulin, 1 μ g/ml hFGF, 50mg/ml gentamycin, 50 μ g/ml Amphotericin B, 5%FBS. After incubation at 37°C for at least 4-5 hours culture media is aspirated and replaced with growth arrest media. Growth arrest media for NHDF contains fibroblast basal media, 50mg/ml gentamycin, 2% FBS, while growth arrest media
25 for AoSMC contains SM basal media, 50mg/ml gentamycin, 50 μ g/ml Amphotericin B, 0.4% FBS. Incubate at 37 °C until day 2.

On day 2, serial dilutions and templates of the polypeptide of interest are designed such that they always include media controls and known-protein controls. For both stimulation and inhibition experiments, proteins are diluted in growth arrest media. For inhibition experiments,
30 TNF α is added to a final concentration of 2ng/ml (NHDF) or 5ng/ml (AoSMC). Add 1/3 vol media containing controls or polypeptides of the present invention and incubate at 37 degrees C/5% CO $_2$ until day 5.

Transfer 60 μ l from each well to another labeled 96-well plate, cover with a plate-sealer, and store at 4 degrees C until Day 6 (for IL6 ELISA). To the remaining 100 μ l in the cell culture
35 plate, aseptically add Alamar Blue in an amount equal to 10% of the culture volume (10 μ l).

Return plates to incubator for 3 to 4 hours. Then measure fluorescence with excitation at 530nm and emission at 590nm using the CytoFluor. This yields the growth stimulation/inhibition data.

On day 5, the IL6 ELISA is performed by coating a 96 well plate with 50-100 μ l/well of Anti-Human IL6 Monoclonal antibody diluted in PBS, pH 7.4, incubate ON at room temperature.

- 5 On day 6, empty the plates into the sink and blot on paper towels. Prepare Assay Buffer containing PBS with 4% BSA. Block the plates with 200 μ l/well of Pierce Super Block blocking buffer in PBS for 1-2 hr and then wash plates with wash buffer (PBS, 0.05% Tween-20). Blot plates on paper towels. Then add 50 μ l/well of diluted Anti-Human IL-6 Monoclonal, Biotin-labeled antibody at 0.50 mg/ml. Make dilutions of IL-6 stock in media (30, 10, 3, 1, 0.3, 0 ng/ml).
- 10 Add duplicate samples to top row of plate. Cover the plates and incubate for 2 hours at RT on shaker.

Plates are washed with wash buffer and blotted on paper towels. Dilute EU-labeled Streptavidin 1:1000 in Assay buffer, and add 100 μ l/well. Cover the plate and incubate 1 h at RT. Plates are again washed with wash buffer and blotted on paper towels.

- 15 Add 100 μ l/well of Enhancement Solution. Shake for 5 minutes. Read the plate on the Wallac DELFIA Fluorometer. Readings from triplicate samples in each assay were tabulated and averaged.

- A positive result in this assay suggests AoSMC cell proliferation and that the polypeptide of the present invention may be involved in dermal fibroblast proliferation and/or smooth muscle cell proliferation. A positive result also suggests many potential uses of polypeptides, polynucleotides, agonists and/or antagonists of the polynucleotide/polypeptide of the present invention which gives a positive result. For example, inflammation and immune responses, wound healing, and angiogenesis, as detailed throughout this specification. Particularly, polypeptides of the present invention and polynucleotides of the present invention may be used in wound healing and dermal regeneration, as well as the promotion of vasculogenesis, both of the blood vessels and lymphatics. The growth of vessels can be used in the treatment of, for example, cardiovascular diseases. Additionally, antagonists of polypeptides and polynucleotides of the invention may be useful in treating diseases, disorders, and/or conditions which involve angiogenesis by acting as an anti-vascular agent (e.g., anti-angiogenesis). These diseases, disorders, and/or conditions are known in the art and/or are described herein, such as, for example, malignancies, solid tumors, benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; arteriosclerotic plaques; ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uveitis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid arthritis; psoriasis; delayed wound healing; endometriosis;
- 20
- 25
- 30
- 35

vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque neovascularization; telangiectasia; hemophiliac joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis. Moreover, antagonists of polypeptides and polynucleotides of the invention may be useful in treating anti-hyperproliferative diseases and/or anti-inflammatory known in the art and/or described herein.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof.

Example 43: Cellular Adhesion Molecule (CAM) Expression on Endothelial Cells

The recruitment of lymphocytes to areas of inflammation and angiogenesis involves specific receptor-ligand interactions between cell surface adhesion molecules (CAMs) on lymphocytes and the vascular endothelium. The adhesion process, in both normal and pathological settings, follows a multi-step cascade that involves intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and endothelial leukocyte adhesion molecule-1 (E-selectin) expression on endothelial cells (EC). The expression of these molecules and others on the vascular endothelium determines the efficiency with which leukocytes may adhere to the local vasculature and extravasate into the local tissue during the development of an inflammatory response. The local concentration of cytokines and growth factor participate in the modulation of the expression of these CAMs.

Briefly, endothelial cells (e.g., Human Umbilical Vein Endothelial cells (HUVECs)) are grown in a standard 96 well plate to confluence, growth medium is removed from the cells and replaced with 100 μ l of 199 Medium (10% fetal bovine serum (FBS)). Samples for testing and positive or negative controls are added to the plate in triplicate (in 10 μ l volumes). Plates are then incubated at 37°C for either 5 h (selectin and integrin expression) or 24 h (integrin expression only). Plates are aspirated to remove medium and 100 μ l of 0.1% paraformaldehyde-PBS(with Ca++ and Mg++) is added to each well. Plates are held at 4°C for 30 min. Fixative is removed from the wells and wells are washed 1X with PBS(+Ca,Mg) + 0.5% BSA and drained. 10 μ l of diluted primary antibody is added to the test and control wells. Anti-ICAM-1-Biotin, Anti-VCAM-1-Biotin and Anti-E-selectin-Biotin are used at a concentration of 10 μ g/ml (1:10 dilution of 0.1 mg/ml stock antibody). Cells are incubated at 37°C for 30 min. in a humidified

environment. Wells are washed three times with PBS(+Ca,Mg) + 0.5% BSA. 20 μ l of diluted ExtrAvidin-Alkaline Phosphatase (1:5,000 dilution, referred to herein as the working dilution) are added to each well and incubated at 37°C for 30 min. Wells are washed three times with PBS(+Ca,Mg)+0.5% BSA. Dissolve 1 tablet of p-Nitrophenol Phosphate pNPP per 5 ml of glycine buffer (pH 10.4). 100 μ l of pNPP substrate in glycine buffer is added to each test well. Standard wells in triplicate are prepared from the working dilution of the ExtrAvidin-Alkaline Phosphatase in glycine buffer: 1:5,000 (10^0) > $10^{0.5}$ > 10^{-1} > $10^{-1.5}$. 5 μ l of each dilution is added to triplicate wells and the resulting AP content in each well is 5.50 ng, 1.74 ng, 0.55 ng, 0.18 ng. 100 μ l of pNPP reagent is then added to each of the standard wells. The plate is incubated at 37°C for 4h. A volume of 50 μ l of 3M NaOH is added to all wells. The plate is read on a plate reader at 405 nm using the background subtraction option on blank wells filled with glycine buffer only. Additionally, the template is set up to indicate the concentration of AP-conjugate in each standard well [5.50 ng; 1.74 ng; 0.55 ng; 0.18 ng]. Results are indicated as amount of bound AP-conjugate in each sample.

Example 44: Alamar Blue Endothelial Cells Proliferation Assay

This assay may be used to quantitatively determine protein mediated inhibition of bFGF-induced proliferation of Bovine Lymphatic Endothelial Cells (LECs), Bovine Aortic Endothelial Cells (BAECs) or Human Microvascular Uterine Myometrial Cells (UTMECs). This assay incorporates a fluorometric growth indicator based on detection of metabolic activity. A standard Alamar Blue Proliferation Assay is prepared in EGM-2MV with 10 ng /ml of bFGF added as a source of endothelial cell stimulation. This assay may be used with a variety of endothelial cells with slight changes in growth medium and cell concentration. Dilutions of the protein batches to be tested are diluted as appropriate. Serum-free medium (GIBCO SFM) without bFGF is used as a non-stimulated control and Angiostatin or TSP-1 are included as a known inhibitory controls.

Briefly, LEC, BAECs or UTMECs are seeded in growth media at a density of 5000 to 2000 cells/well in a 96 well plate and placed at 37 degreesC overnight. After the overnight incubation of the cells, the growth media is removed and replaced with GIBCO EC-SFM. The cells are treated with the appropriate dilutions of the protein of interest or control protein sample(s) (prepared in SFM) in triplicate wells with additional bFGF to a concentration of 10 ng/ ml. Once the cells have been treated with the samples, the plate(s) is/are placed back in the 37° C incubator for three days. After three days 10 ml of stock alamar blue (Biosource Cat# DAL1100) is added to each well and the plate(s) is/are placed back in the 37°C incubator for four hours. The plate(s) are

then read at 530nm excitation and 590nm emission using the CytoFluor fluorescence reader. Direct output is recorded in relative fluorescence units.

Alamar blue is an oxidation-reduction indicator that both fluoresces and changes color in response to chemical reduction of growth medium resulting from cell growth. As cells grow in culture, innate metabolic activity results in a chemical reduction of the immediate surrounding environment. Reduction related to growth causes the indicator to change from oxidized (non-fluorescent blue) form to reduced (fluorescent red) form (i.e., stimulated proliferation will produce a stronger signal and inhibited proliferation will produce a weaker signal and the total signal is proportional to the total number of cells as well as their metabolic activity). The background level of activity is observed with the starvation medium alone. This is compared to the output observed from the positive control samples (bFGF in growth medium) and protein dilutions.

Example 45: Detection of Inhibition of a Mixed Lymphocyte Reaction

This assay can be used to detect and evaluate inhibition of a Mixed Lymphocyte Reaction (MLR) by gene products (e.g., isolated polypeptides). Inhibition of a MLR may be due to a direct effect on cell proliferation and viability, modulation of costimulatory molecules on interacting cells, modulation of adhesiveness between lymphocytes and accessory cells, or modulation of cytokine production by accessory cells. Multiple cells may be targeted by these polypeptides since the peripheral blood mononuclear fraction used in this assay includes T, B and natural killer lymphocytes, as well as monocytes and dendritic cells.

Polypeptides of interest found to inhibit the MLR may find application in diseases associated with lymphocyte and monocyte activation or proliferation. These include, but are not limited to, diseases such as asthma, arthritis, diabetes, inflammatory skin conditions, psoriasis, eczema, systemic lupus erythematosus, multiple sclerosis, glomerulonephritis, inflammatory bowel disease, crohn's disease, ulcerative colitis, arteriosclerosis, cirrhosis, graft vs. host disease, host vs. graft disease, hepatitis, leukemia and lymphoma.

Briefly, PBMCs from human donors are purified by density gradient centrifugation using Lymphocyte Separation Medium (LSM[®], density 1.0770 g/ml, Organon Teknika Corporation, West Chester, PA). PBMCs from two donors are adjusted to 2×10^6 cells/ml in RPMI-1640 (Life Technologies, Grand Island, NY) supplemented with 10% FCS and 2 mM glutamine. PBMCs from a third donor is adjusted to 2×10^5 cells/ml. Fifty microliters of PBMCs from each donor is added to wells of a 96-well round bottom microtiter plate. Dilutions of test materials (50 μ l) is added in triplicate to microtiter wells. Test samples (of the protein of interest) are added for final dilution of 1:4; rhuIL-2 (R&D Systems, Minneapolis, MN, catalog number 202-IL) is added to a

final concentration of 1 $\mu\text{g/ml}$; anti-CD4 mAb (R&D Systems, clone 34930.11, catalog number MAB379) is added to a final concentration of 10 $\mu\text{g/ml}$. Cells are cultured for 7-8 days at 37°C in 5% CO₂, and 1 μCi of [³H] thymidine is added to wells for the last 16 hrs of culture. Cells are harvested and thymidine incorporation determined using a Packard TopCount. Data is expressed as the mean and standard deviation of triplicate determinations.

Samples of the protein of interest are screened in separate experiments and compared to the negative control treatment, anti-CD4 mAb, which inhibits proliferation of lymphocytes and the positive control treatment, IL-2 (either as recombinant material or supernatant), which enhances proliferation of lymphocytes.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof.

Example 46: Assays for Protease Activity

The following assay may be used to assess protease activity of the polypeptides of the invention.

Gelatin and casein zymography are performed essentially as described (Heusen et al., *Anal. Biochem.*, 102:196-202 (1980); Wilson et al., *Journal of Urology*, 149:653-658 (1993)). Samples are run on 10% polyacryamide/0.1% SDS gels containing 1% gelatin or casein, soaked in 2.5% triton at room temperature for 1 hour, and in 0.1M glycine, pH 8.3 at 37°C 5 to 16 hours. After staining in amido black areas of proteolysis appear as clear areas against the blue-black background. Trypsin (Sigma T8642) is used as a positive control.

Protease activity is also determined by monitoring the cleavage of n-a-benzoyl-L-arginine ethyl ester (BAEE) (Sigma B-4500. Reactions are set up in (25mMNaPO₄, 1mM EDTA, and 1mM BAEE), pH 7.5. Samples are added and the change in adsorbance at 260nm is monitored on the Beckman DU-6 spectrophotometer in the time-drive mode. Trypsin is used as a positive control.

Additional assays based upon the release of acid-soluble peptides from casein or hemoglobin measured as adsorbance at 280 nm or colorimetrically using the Folin method are performed as described in Bergmeyer, et al., *Methods of Enzymatic Analysis*, 5 (1984). Other assays involve the solubilization of chromogenic substrates (Ward, *Applied Science*, 251-317 (1983)).

Example 47: Identifying Serine Protease Substrate Specificity

Methods known in the art or described herein may be used to determine the substrate specificity of the polypeptides of the present invention having serine protease activity. A preferred method of determining substrate specificity is by the use of positional scanning synthetic combinatorial libraries as described in GB 2 324 529 (incorporated herein in its entirety).

Example 48: Ligand Binding Assays

The following assay may be used to assess ligand binding activity of the polypeptides of the invention.

Ligand binding assays provide a direct method for ascertaining receptor pharmacology and are adaptable to a high throughput format. The purified ligand for a polypeptide is radiolabeled to high specific activity (50-2000 Ci/mmol) for binding studies. A determination is then made that the process of radiolabeling does not diminish the activity of the ligand towards its polypeptide. Assay conditions for buffers, ions, pH and other modulators such as nucleotides are optimized to establish a workable signal to noise ratio for both membrane and whole cell polypeptide sources. For these assays, specific polypeptide binding is defined as total associated radioactivity minus the radioactivity measured in the presence of an excess of unlabeled competing ligand. Where possible, more than one competing ligand is used to define residual nonspecific binding.

Example 49: Functional Assay in *Xenopus* Oocytes

Capped RNA transcripts from linearized plasmid templates encoding the polypeptides of the invention are synthesized in vitro with RNA polymerases in accordance with standard procedures. In vitro transcripts are suspended in water at a final concentration of 0.2 mg/ml. Ovarian lobes are removed from adult female toads, Stage V defolliculated oocytes are obtained, and RNA transcripts (10 ng/oocyte) are injected in a 50 nl bolus using a microinjection apparatus. Two electrode voltage clamps are used to measure the currents from individual *Xenopus oocytes* in response polypeptides and polypeptide agonist exposure. Recordings are made in Ca²⁺ free Barth's medium at room temperature. The *Xenopus* system can be used to screen known ligands and tissue/cell extracts for activating ligands.

Example 50: Microphysiometric Assays

Activation of a wide variety of secondary messenger systems results in extrusion of small amounts of acid from a cell. The acid formed is largely as a result of the increased metabolic activity required to fuel the intracellular signaling process. The pH changes in the media surrounding the cell are very small but are detectable by the CYTOSENSOR microphysiometer (Molecular Devices Ltd., Menlo Park, Calif.). The CYTOSENSOR is thus capable of detecting the activation of polypeptide which is coupled to an energy utilizing intracellular signaling pathway.

Example 51: Extract/Cell Supernatant Screening

A large number of mammalian receptors exist for which there remains, as yet, no cognate activating ligand (agonist). Thus, active ligands for these receptors may not be included within the ligands banks as identified to date. Accordingly, the polypeptides of the invention can also be functionally screened (using calcium, cAMP, microphysiometer, oocyte electrophysiology, etc., functional screens) against tissue extracts to identify its natural ligands. Extracts that produce positive functional responses can be sequentially subfractionated until an activating ligand is isolated and identified.

Example 52: Calcium and cAMP Functional Assays

Seven transmembrane receptors which are expressed in HEK 293 cells have been shown to be coupled functionally to activation of PLC and calcium mobilization and/or cAMP stimulation or inhibition. Basal calcium levels in the HEK 293 cells in receptor-transfected or vector control cells were observed to be in the normal, 100 nM to 200 nM, range. HEK 293 cells expressing recombinant receptors are loaded with fura 2 and in a single day >150 selected ligands or tissue/cell extracts are evaluated for agonist induced calcium mobilization. Similarly, HEK 293 cells expressing recombinant receptors are evaluated for the stimulation or inhibition of cAMP production using standard cAMP quantitation assays. Agonists presenting a calcium transient or cAMP fluctuation are tested in vector control cells to determine if the response is unique to the transfected cells expressing receptor.

Example 53: ATP-binding assay

The following assay may be used to assess ATP-binding activity of polypeptides of the invention.

ATP-binding activity of the polypeptides of the invention may be detected using the ATP-binding assay described in U.S. Patent 5,858,719, which is herein incorporated by reference in its entirety. Briefly, ATP-binding to polypeptides of the invention is measured via photoaffinity labeling with 8-azido-ATP in a competition assay. Reaction mixtures containing 1 mg/ml of the ABC transport protein of the present invention are incubated with varying concentrations of ATP, or the non-hydrolyzable ATP analog adenylyl-5'-imidodiphosphate for 10 minutes at 4°C. A mixture of 8-azido-ATP (Sigma Chem. Corp., St. Louis, MO.) plus 8-azido-ATP (³²P-ATP) (5 mCi/μmol, ICN, Irvine CA.) is added to a final concentration of 100 μM and 0.5 ml aliquots are placed in the wells of a porcelain spot plate on ice. The plate is irradiated using a short wave 254 nm UV lamp at a distance of 2.5 cm from the plate for two one-minute intervals with a one-minute cooling interval in between. The reaction is stopped by addition of dithiothreitol to a final concentration of 2mM. The incubations are subjected to SDS-PAGE electrophoresis, dried, and autoradiographed. Protein bands corresponding to the particular polypeptides of the invention are excised, and the radioactivity quantified. A decrease in radioactivity with increasing ATP or adenylyl-5'-imidodiphosphate provides a measure of ATP affinity to the polypeptides.

Example 54: Small Molecule Screening

This invention is particularly useful for screening therapeutic compounds by using the polypeptides of the invention, or binding fragments thereof, in any of a variety of drug screening techniques. The polypeptide or fragment employed in such a test may be affixed to a solid support, expressed on a cell surface, free in solution, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. One may measure, for example, the formulation of complexes between the agent being tested and polypeptide of the invention.

Thus, the present invention provides methods of screening for drugs or any other agents which affect activities mediated by the polypeptides of the invention. These methods comprise contacting such an agent with a polypeptide of the invention or fragment thereof and assaying for the presence of a complex between the agent and the polypeptide or fragment thereof, by methods well known in the art. In such a competitive binding assay, the agents to screen are typically labeled. Following incubation, free agent is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of a particular agent to bind to the polypeptides of the invention.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to the polypeptides of the invention, and is described in great detail in European Patent Application 84/03564, published on September 13, 1984, which is herein incorporated by reference in its entirety. Briefly stated, large numbers of different small molecule
5 test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. The test compounds are reacted with polypeptides of the invention and washed. Bound polypeptides are then detected by methods well known in the art. Purified polypeptides are coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies may be used to capture the peptide and immobilize it on the solid support.

10 This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding polypeptides of the invention specifically compete with a test compound for binding to the polypeptides or fragments thereof. In this manner, the antibodies are used to detect the presence of any peptide which shares one or more antigenic epitopes with a polypeptide of the invention.

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Example 55: Phosphorylation Assay

In order to assay for phosphorylation activity of the polypeptides of the invention, a phosphorylation assay as described in U.S. Patent 5,958,405 (which is herein incorporated by
20 reference) is utilized. Briefly, phosphorylation activity may be measured by phosphorylation of a protein substrate using gamma-labeled ^{32}P -ATP and quantitation of the incorporated radioactivity using a gamma radioisotope counter. The polypeptides of the invention are incubated with the protein substrate, ^{32}P -ATP, and a kinase buffer. The ^{32}P incorporated into the substrate is then separated from free ^{32}P -ATP by electrophoresis, and the incorporated ^{32}P is counted and compared
25 to a negative control. Radioactivity counts above the negative control are indicative of phosphorylation activity of the polypeptides of the invention.

Example 56: Detection of Phosphorylation Activity (Activation) of the Polypeptides of the Invention in the Presence of Polypeptide Ligands

30 Methods known in the art or described herein may be used to determine the phosphorylation activity of the polypeptides of the invention. A preferred method of determining phosphorylation activity is by the use of the tyrosine phosphorylation assay as described in US 5,817,471 (incorporated herein by reference).

***Example 57: Identification Of Signal Transduction Proteins That Interact With
Polypeptides Of The Present Invention***

5 The purified polypeptides of the invention are research tools for the identification, characterization and purification of additional signal transduction pathway proteins or receptor proteins. Briefly, labeled polypeptides of the invention are useful as reagents for the purification of molecules with which it interacts. In one embodiment of affinity purification, polypeptides of the invention are covalently coupled to a chromatography column. Cell-free extract derived from
10 putative target cells, such as carcinoma tissues, is passed over the column, and molecules with appropriate affinity bind to the polypeptides of the invention. The protein complex is recovered from the column, dissociated, and the recovered molecule subjected to N-terminal protein sequencing. This amino acid sequence is then used to identify the captured molecule or to design degenerate oligonucleotide probes for cloning the relevant gene from an appropriate cDNA library.

15

Example 58: IL-6 Bioassay

 To test the proliferative effects of the polypeptides of the invention, the IL-6 Bioassay as described by Marz *et al.* is utilized (*Proc. Natl. Acad. Sci., U.S.A.*, 95:3251-56 (1998), which is
20 herein incorporated by reference). Briefly, IL-6 dependent B9 murine cells are washed three times in IL-6 free medium and plated at a concentration of 5,000 cells per well in 50 μ l, and 50 μ l of the IL-6-like polypeptide is added. After 68 hrs. at 37°C, the number of viable cells is measured by adding the tetrazolium salt thiazolyl blue (MTT) and incubating for a further 4 hrs. at 37°C. B9 cells are lysed by SDS and optical density is measured at 570 nm. Controls containing IL-6
25 (positive) and no cytokine (negative) are utilized. Enhanced proliferation in the test sample(s) relative to the negative control is indicative of proliferative effects mediated by polypeptides of the invention.

Example 59: Support of Chicken Embryo Neuron Survival

30

 To test whether sympathetic neuronal cell viability is supported by polypeptides of the invention, the chicken embryo neuronal survival assay of Senaldi *et al* is utilized (*Proc. Natl. Acad. Sci., U.S.A.*, 96:11458-63 (1998), which is herein incorporated by reference). Briefly, motor and sympathetic neurons are isolated from chicken embryos, resuspended in L15 medium (with
35 10% FCS, glucose, sodium selenite, progesterone, conalbumin, putrescine, and insulin; Life

Technologies, Rockville, MD.) and Dulbecco's modified Eagles medium [with 10% FCS, glutamine, penicillin, and 25 mM Hepes buffer (pH 7.2); Life Technologies, Rockville, MD.], respectively, and incubated at 37°C in 5% CO₂ in the presence of different concentrations of the purified IL-6-like polypeptide, as well as a negative control lacking any cytokine. After 3 days, neuron survival is determined by evaluation of cellular morphology, and through the use of the colorimetric assay of Mosmann (Mosmann, T., *J. Immunol. Methods*, 65:55-63 (1983)). Enhanced neuronal cell viability as compared to the controls lacking cytokine is indicative of the ability of the inventive purified IL-6-like polypeptide(s) to enhance the survival of neuronal cells.

10 *Example 60: Assay for Phosphatase Activity*

The following assay may be used to assess serine/threonine phosphatase (PTPase) activity of the polypeptides of the invention.

In order to assay for serine/threonine phosphatase (PTPase) activity, assays can be utilized which are widely known to those skilled in the art. For example, the serine/threonine phosphatase (PSPase) activity is measured using a PSPase assay kit from New England Biolabs, Inc. Myelin basic protein (MyBP), a substrate for PSPase, is phosphorylated on serine and threonine residues with cAMP-dependent Protein Kinase in the presence of [³²P]ATP. Protein serine/threonine phosphatase activity is then determined by measuring the release of inorganic phosphate from ³²P-labeled MyBP.

Example 61: Interaction of Serine/Threonine Phosphatases with other Proteins

The polypeptides of the invention with serine/threonine phosphatase activity as determined in Example 60 are research tools for the identification, characterization and purification of additional interacting proteins or receptor proteins, or other signal transduction pathway proteins. Briefly, labeled polypeptide(s) of the invention is useful as a reagent for the purification of molecules with which it interacts. In one embodiment of affinity purification, polypeptide of the invention is covalently coupled to a chromatography column. Cell-free extract derived from putative target cells, such as neural or liver cells, is passed over the column, and molecules with appropriate affinity bind to the polypeptides of the invention. The polypeptides of the invention - complex is recovered from the column, dissociated, and the recovered molecule subjected to N-terminal protein sequencing. This amino acid sequence is then used to identify the captured molecule or to design degenerate oligonucleotide probes for cloning the relevant gene from an appropriate cDNA library.

Example 62: Assaying for Heparanase Activity

In order to assay for heparanase activity of the polypeptides of the invention, the
5 heparanase assay described by Vlodavsky et al is utilized (Vlodavsky, I., et al., Nat. Med., 5:793-
802 (1999)). Briefly, cell lysates, conditioned media or intact cells (1×10^6 cells per 35-mm dish)
are incubated for 18 hrs at 37°C, pH 6.2-6.6, with ^{35}S -labeled ECM or soluble ECM derived peak I
proteoglycans. The incubation medium is centrifuged and the supernatant is analyzed by gel
10 filtration on a Sepharose CL-6B column (0.9 x 30 cm). Fractions are eluted with PBS and their
radioactivity is measured. Degradation fragments of heparan sulfate side chains are eluted from
Sepharose 6B at $0.5 < K_{av} < 0.8$ (peak II). Each experiment is done at least three times.
Degradation fragments corresponding to "peak II," as described by Vlodavsky et al., is indicative
of the activity of the polypeptides of the invention in cleaving heparan sulfate.

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Example 63: Immobilization of biomolecules

This example provides a method for the stabilization of polypeptides of the invention in
non-host cell lipid bilayer constructs (see, e.g., Bieri et al., Nature Biotech 17:1105-1108 (1999),
hereby incorporated by reference in its entirety herein) which can be adapted for the study of
20 polypeptides of the invention in the various functional assays described above. Briefly,
carbohydrate-specific chemistry for biotinylation is used to confine a biotin tag to the extracellular
domain of the polypeptides of the invention, thus allowing uniform orientation upon
immobilization. A 50uM solution of polypeptides of the invention in washed membranes is
incubated with 20 mM NaIO₄ and 1.5 mg/ml (4mM) BACH or 2 mg/ml (7.5mM) biotin-
25 hydrazide for 1 hr at room temperature (reaction volume, 150ul). Then the sample is dialyzed
(Pierce Slidealizer Cassett, 10 kDa cutoff; Pierce Chemical Co., Rockford IL) at 4C first for 5 h,
exchanging the buffer after each hour, and finally for 12 h against 500 ml buffer R (0.15 M NaCl,
1 mM MgCl₂, 10 mM sodium phosphate, pH7). Just before addition into a cuvette, the sample is
diluted 1:5 in buffer ROG50 (Buffer R supplemented with 50 mM octylglucoside).

30

Example 64: TAQMAN

Quantitative PCR (QPCR). Total RNA from cells in culture are extracted by Trizol
35 separation as recommended by the supplier (LifeTechnologies). (Total RNA is treated with DNase

I (Life Technologies) to remove any contaminating genomic DNA before reverse transcription.) Total RNA (50 ng) is used in a one-step, 50ul, RT-QPCR, consisting of Taqman Buffer A (Perkin-Elmer; 50 mM KCl/10 mM Tris, pH 8.3), 5.5 mM MgCl₂, 240 μM each dNTP, 0.4 units RNase inhibitor(Promega), 8%glycerol, 0.012% Tween-20, 0.05% gelatin, 0.3uM primers, 0.1uM probe, 5 0.025units Amplitaq Gold (Perkin-Elmer) and 2.5 units Superscript II reverse transcriptase (Life Technologies). As a control for genomic contamination, parallel reactions are setup without reverse transcriptase. The relative abundance of (unknown) and 18S RNAs are assessed by using the Applied Biosystems Prism 7700 Sequence Detection System (Livak, K. J., Flood, S. J., Marmaro, J., Giusti, W. & Deetz, K. (1995) PCR Methods Appl. 4, 357-362). Reactions are 10 carried out at 48°C for 30 min, 95°C for 10 min, followed by 40 cycles of 95°C for 15s, 60°C for 1 min. Reactions are performed in triplicate.

Primers (f & r) and FRET probes sets are designed using Primer Express Software (Perkin-Elmer). Probes are labeled at the 5'-end with the reporter dye 6-FAM and on the 3'-end with the quencher dye TAMRA (Biosource International, Camarillo, CA or Perkin-Elmer).

15

Example 65: Assays for Metalloproteinase Activity

Metalloproteinases (EC 3.4.24.-) are peptide hydrolases which use metal ions, such as Zn²⁺, as the catalytic mechanism. Metalloproteinase activity of polypeptides of the present 20 invention can be assayed according to the following methods.

Proteolysis of alpha-2-macroglobulin

To confirm protease activity, purified polypeptides of the invention are mixed with the substrate alpha-2-macroglobulin (0.2 unit/ml; Boehringer Mannheim, Germany) in 1x assay buffer 25 (50 mM HEPES, pH 7.5, 0.2 M NaCl, 10 mM CaCl₂, 25 μM ZnCl₂ and 0.05% Brij-35) and incubated at 37°C for 1-5 days. Trypsin is used as positive control. Negative controls contain only alpha-2-macroglobulin in assay buffer. The samples are collected and boiled in SDS-PAGE sample buffer containing 5% 2-mercaptoethanol for 5-min, then loaded onto 8% SDS-polyacrylamide gel. After electrophoresis the proteins are visualized by silver staining. Proteolysis 30 is evident by the appearance of lower molecular weight bands as compared to the negative control.

Inhibition of alpha-2-macroglobulin proteolysis by inhibitors of metalloproteinases

Known metalloproteinase inhibitors (metal chelators (EDTA, EGTA, AND HgCl₂), peptide metalloproteinase inhibitors (TIMP-1 and TIMP-2), and commercial small molecule MMP 35 inhibitors) are used to characterize the proteolytic activity of polypeptides of the invention. The

three synthetic MMP inhibitors used are: MMP inhibitor I, [$IC_{50} = 1.0 \mu M$ against MMP-1 and MMP-8; $IC_{50} = 30 \mu M$ against MMP-9; $IC_{50} = 150 \mu M$ against MMP-3]; MMP-3 (stromelysin-1) inhibitor I [$IC_{50} = 5 \mu M$ against MMP-3], and MMP-3 inhibitor II [$K_i = 130 nM$ against MMP-3]; inhibitors available through Calbiochem, catalog # 444250, 444218, and 444225, respectively).

- 5 Briefly, different concentrations of the small molecule MMP inhibitors are mixed with purified polypeptides of the invention ($50 \mu g/ml$) in $22.9 \mu l$ of 1x HEPES buffer (50 mM HEPES, pH 7.5, 0.2 M NaCl, 10 mM $CaCl_2$, 25 μM $ZnCl_2$ and 0.05%Brij-35) and incubated at room temperature ($24^\circ C$) for 2-hr, then $7.1 \mu l$ of substrate alpha-2-macroglobulin (0.2 unit/ml) is added and incubated at $37^\circ C$ for 20-hr. The reactions are stopped by adding 4x sample buffer and boiled
10 immediately for 5 minutes. After SDS-PAGE, the protein bands are visualized by silver stain.

Synthetic Fluorogenic Peptide Substrates Cleavage Assay

- The substrate specificity for polypeptides of the invention with demonstrated metalloproteinase activity can be determined using synthetic fluorogenic peptide substrates
15 (purchased from BACHEM Bioscience Inc). Test substrates include, M-1985, M-2225, M-2105, M-2110, and M-2255. The first four are MMP substrates and the last one is a substrate of tumor necrosis factor- α (TNF- α) converting enzyme (TACE). All the substrates are prepared in 1:1 dimethyl sulfoxide (DMSO) and water. The stock solutions are 50-500 μM . Fluorescent assays are performed by using a Perkin Elmer LS 50B luminescence spectrometer equipped with a constant
20 temperature water bath. The excitation λ is 328 nm and the emission λ is 393 nm. Briefly, the assay is carried out by incubating $176 \mu l$ 1x HEPES buffer (0.2 M NaCl, 10 mM $CaCl_2$, 0.05% Brij-35 and 50 mM HEPES, pH 7.5) with $4 \mu l$ of substrate solution (50 μM) at $25^\circ C$ for 15 minutes, and then adding $20 \mu l$ of a purified polypeptide of the invention into the assay cuvet. The final concentration of substrate is 1 μM . Initial hydrolysis rates are monitored for 30-min.

25

Example 66: Characterization of the cDNA contained in a deposited plasmid

- The size of the cDNA insert contained in a deposited plasmid may be routinely determined
30 using techniques known in the art, such as PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the cDNA sequence. For example, two primers of 17-30 nucleotides derived from each end of the cDNA (i.e., hybridizable to the absolute 5' nucleotide or the 3' nucleotide end of the sequence of SEQ ID NO:X, respectively) are synthesized and used to amplify the cDNA using the deposited cDNA plasmid as a template. The polymerase chain

reaction is carried out under routine conditions, for instance, in 25 ul of reaction mixture with 0.5 ug of the above cDNA template. A convenient reaction mixture is 1.5-5 mM MgCl₂, 0.01% (w/v) gelatin, 20 uM each of dATP, dCTP, dGTP, dTTP, 25 pmol of each primer and 0.25 Unit of Taq polymerase. Thirty five cycles of PCR (denaturation at 94 degree C for 1 min; annealing at 55
5 degree C for 1 min; elongation at 72 degree C for 1 min) are performed with a Perkin-Elmer Cetus automated thermal cyclers. The amplified product is analyzed by agarose gel electrophoresis. The PCR product is verified to be the selected sequence by subcloning and sequencing the DNA product. It will be clear that the invention may be practiced otherwise than as particularly described in the foregoing description and examples. Numerous modifications and variations of the present
10 invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

Incorporation by Reference

The entire disclosure of each document cited (including patents, patent applications,
15 journal articles, abstracts, laboratory manuals, books, or other disclosures) in the Background of the Invention, Detailed Description, and Examples is hereby incorporated herein by reference. In addition, the sequence listing submitted herewith is incorporated herein by reference in its entirety. The specification and sequence listing of each of the following U.S. and PCT applications are herein incorporated by reference in their entirety: U.S. Appln. No. 60/040,162 filed on 07-Mar-
20 1997, U.S. Appln. No. 60/043,576 filed on 11-Apr-1997, U.S. Appln. No. 60/047,601 filed on 23-May-1997, U.S. Appln. No. 60/056,845 filed on 22-Aug-1997, U.S. Appln. No. 60/043,580 filed on 11-Apr-1997, U.S. Appln. No. 60/047,599 filed on 23-May-1997, U.S. Appln. No. 60/056,664 filed on 22-Aug-1997, U.S. Appln. No. 60/043,314 filed on 11-Apr-1997, U.S. Appln. No. 60/047,632 filed on 23-May-1997, U.S. Appln. No. 60/056,892 filed on 22-Aug-1997, U.S. Appln.
25 No. 60/043,568 filed on 11-Apr-1997, U.S. Appln. No. 60/047,595 filed on 23-May-1997, U.S. Appln. No. 60/056,632 filed on 22-Aug-1997, U.S. Appln. No. 60/043,578 filed on 11-Apr-1997, U.S. Appln. No. 60/040,333 filed on 07-Mar-1997, U.S. Appln. No. 60/043,670 filed on 11-Apr-1997, U.S. Appln. No. 60/047,596 filed on 23-May-1997, U.S. Appln. No. 60/056,864 filed on 22-Aug-1997, U.S. Appln. No. 60/043,674 filed on 11-Apr-1997, U.S. Appln. No. 60/047,612 filed
30 on 23-May-1997, U.S. Appln. No. 60/056,631 filed on 22-Aug-1997, U.S. Appln. No. 60/043,569 filed on 11-Apr-1997, U.S. Appln. No. 60/047,588 filed on 23-May-1997, U.S. Appln. No. 60/056,876 filed on 22-Aug-1997, U.S. Appln. No. 60/043,671 filed on 11-Apr-1997, U.S. Appln. No. 60/043,311 filed on 11-Apr-1997, U.S. Appln. No. 60/038,621 filed on 07-Mar-1997, U.S. Appln. No. 60/043,672 filed on 11-Apr-1997, U.S. Appln. No. 60/047,613 filed on 23-May-1997,
35 U.S. Appln. No. 60/056,636 filed on 22-Aug-1997, U.S. Appln. No. 60/043,669 filed on 11-Apr-

1997, U.S. Appln. No. 60/047,582 filed on 23-May-1997, U.S. Appln. No. 60/056,910 filed on 22-Aug-1997, U.S. Appln. No. 60/043,315 filed on 11-Apr-1997, U.S. Appln. No. 60/047,598 filed on 23-May-1997, U.S. Appln. No. 60/056,874 filed on 22-Aug-1997, U.S. Appln. No. 60/043,312 filed on 11-Apr-1997, U.S. Appln. No. 60/047,585 filed on 23-May-1997, U.S. Appln. No. 5 60/056,881 filed on 22-Aug-1997, U.S. Appln. No. 60/043,313 filed on 11-Apr-1997, U.S. Appln. No. 60/047,586 filed on 23-May-1997, U.S. Appln. No. 60/056,909 filed on 22-Aug-1997, U.S. Appln. No. 60/040,161 filed on 07-Mar-1997, U.S. Appln. No. 60/047,587 filed on 23-May-1997, U.S. Appln. No. 60/056,879 filed on 22-Aug-1997, U.S. Appln. No. 60/047,500 filed on 23-May-1997, U.S. Appln. No. 60/056,880 filed on 22-Aug-1997, U.S. Appln. No. 60/047,584 filed on 23-10 May-1997, U.S. Appln. No. 60/056,894 filed on 22-Aug-1997, U.S. Appln. No. 60/047,492 filed on 23-May-1997, U.S. Appln. No. 60/056,911 filed on 22-Aug-1997, U.S. Appln. No. 60/040,626 filed on 07-Mar-1997, U.S. Appln. No. 60/047,503 filed on 23-May-1997, U.S. Appln. No. 60/056,903 filed on 22-Aug-1997, U.S. Appln. No. 60/047,501 filed on 23-May-1997, U.S. Appln. No. 60/056,637 filed on 22-Aug-1997, U.S. Appln. No. 60/047,590 filed on 23-May-1997, U.S. 15 Appln. No. 60/056,875 filed on 22-Aug-1997, U.S. Appln. No. 60/047,581 filed on 23-May-1997, U.S. Appln. No. 60/056,882 filed on 22-Aug-1997, U.S. Appln. No. 60/047,592 filed on 23-May-1997, U.S. Appln. No. 60/056,888 filed on 22-Aug-1997, U.S. Appln. No. 60/040,334 filed on 07-Mar-1997, U.S. Appln. No. 60/047,618 filed on 23-May-1997, U.S. Appln. No. 60/056,872 filed on 22-Aug-1997, U.S. Appln. No. 60/047,617 filed on 23-May-1997, U.S. Appln. No. 60/056,662 20 filed on 22-Aug-1997, U.S. Appln. No. 60/047,589 filed on 23-May-1997, U.S. Appln. No. 60/056,862 filed on 22-Aug-1997, U.S. Appln. No. 60/047,594 filed on 23-May-1997, U.S. Appln. No. 60/056,884 filed on 22-Aug-1997, U.S. Appln. No. 60/047,583 filed on 23-May-1997, U.S. Appln. No. 60/056,878 filed on 22-Aug-1997, U.S. Appln. No. 60/040,336 filed on 07-Mar-1997, U.S. Appln. No. 60/047,502 filed on 23-May-1997, U.S. Appln. No. 60/056,893 filed on 22-Aug-25 1997, U.S. Appln. No. 60/047,633 filed on 23-May-1997, U.S. Appln. No. 60/056,630 filed on 22-Aug-1997, U.S. Appln. No. 60/047,593 filed on 23-May-1997, U.S. Appln. No. 60/056,887 filed on 22-Aug-1997, U.S. Appln. No. 60/040,163 filed on 07-Mar-1997, U.S. Appln. No. 60/047,597 filed on 23-May-1997, U.S. Appln. No. 60/056,889 filed on 22-Aug-1997, U.S. Appln. No. 60/047,615 filed on 23-May-1997, U.S. Appln. No. 60/056,877 filed on 22-Aug-1997, U.S. Appln. 30 No. 60/047,600 filed on 23-May-1997, U.S. Appln. No. 60/056,886 filed on 22-Aug-1997, U.S. Appln. No. 60/047,614 filed on 23-May-1997, U.S. Appln. No. 60/056,908 filed on 22-Aug-1997, U.S. Appln. No. 60/040,710 filed on 14-Mar-1997, U.S. Appln. No. 60/050,934 filed on 30-May-1997, U.S. Appln. No. 60/048,100 filed on 30-May-1997, U.S. Appln. No. 60/040,762 filed on 14-Mar-1997, U.S. Appln. No. 60/048,357 filed on 30-May-1997, U.S. Appln. No. 60/048,189 filed 35 on 30-May-1997, U.S. Appln. No. 60/041,277 filed on 21-Mar-1997, U.S. Appln. No. 60/048,188

filed on 30-May-1997, U.S. Appln. No. 60/048,094 filed on 30-May-1997, U.S. Appln. No. 60/048,350 filed on 30-May-1997, U.S. Appln. No. 60/048,135 filed on 30-May-1997, U.S. Appln. No. 60/042,344 filed on 21-Mar-1997, U.S. Appln. No. 60/048,187 filed on 30-May-1997, U.S. Appln. No. 60/048,099 filed on 30-May-1997, U.S. Appln. No. 60/050,937 filed on 30-May-1997, U.S. Appln. No. 60/048,352 filed on 30-May-1997, U.S. Appln. No. 60/041,276 filed on 21-Mar-1997, U.S. Appln. No. 60/048,069 filed on 30-May-1997, U.S. Appln. No. 60/048,131 filed on 30-May-1997, U.S. Appln. No. 60/048,186 filed on 30-May-1997, U.S. Appln. No. 60/048,095 filed on 30-May-1997, U.S. Appln. No. 60/041,281 filed on 21-Mar-1997, U.S. Appln. No. 60/048,355 filed on 30-May-1997, U.S. Appln. No. 60/048,096 filed on 30-May-1997, U.S. Appln. No. 60/048,351 filed on 30-May-1997, U.S. Appln. No. 60/048,154 filed on 30-May-1997, U.S. Appln. No. 60/048,160 filed on 30-May-1997, U.S. Appln. No. 60/042,825 filed on 08-Apr-1997, U.S. Appln. No. 60/048,070 filed on 30-May-1997, U.S. Appln. No. 60/042,727 filed on 08-Apr-1997, U.S. Appln. No. 60/048,068 filed on 30-May-1997, U.S. Appln. No. 60/042,726 filed on 08-Apr-1997, U.S. Appln. No. 60/048,184 filed on 30-May-1997, U.S. Appln. No. 60/042,728 filed on 08-Apr-1997, U.S. Appln. No. 60/042,754 filed on 08-Apr-1997, U.S. Appln. No. 60/048,190 filed on 30-May-1997, U.S. Appln. No. 60/044,039 filed on 30-May-1997, U.S. Appln. No. 60/048,093 filed on 30-May-1997, U.S. Appln. No. 60/048,885 filed on 06-Jun-1997, U.S. Appln. No. 60/057,645 filed on 05-Sep-1997, U.S. Appln. No. 60/049,375 filed on 06-Jun-1997, U.S. Appln. No. 60/057,642 filed on 05-Sep-1997, U.S. Appln. No. 60/048,881 filed on 06-Jun-1997, U.S. Appln. No. 60/057,668 filed on 05-Sep-1997, U.S. Appln. No. 60/048,880 filed on 06-Jun-1997, U.S. Appln. No. 60/057,635 filed on 05-Sep-1997, U.S. Appln. No. 60/048,896 filed on 06-Jun-1997, U.S. Appln. No. 60/057,627 filed on 05-Sep-1997, U.S. Appln. No. 60/049,020 filed on 06-Jun-1997, U.S. Appln. No. 60/057,667 filed on 05-Sep-1997, U.S. Appln. No. 60/048,876 filed on 06-Jun-1997, U.S. Appln. No. 60/057,666 filed on 05-Sep-1997, U.S. Appln. No. 60/048,895 filed on 06-Jun-1997, U.S. Appln. No. 60/057,764 filed on 05-Sep-1997, U.S. Appln. No. 60/048,884 filed on 06-Jun-1997, U.S. Appln. No. 60/057,643 filed on 05-Sep-1997, U.S. Appln. No. 60/048,894 filed on 06-Jun-1997, U.S. Appln. No. 60/057,769 filed on 05-Sep-1997, U.S. Appln. No. 60/048,971 filed on 06-Jun-1997, U.S. Appln. No. 60/057,763 filed on 05-Sep-1997, U.S. Appln. No. 60/048,964 filed on 06-Jun-1997, U.S. Appln. No. 60/057,650 filed on 05-Sep-1997, U.S. Appln. No. 60/048,882 filed on 06-Jun-1997, U.S. Appln. No. 60/057,584 filed on 05-Sep-1997, U.S. Appln. No. 60/048,899 filed on 06-Jun-1997, U.S. Appln. No. 60/057,647 filed on 05-Sep-1997, U.S. Appln. No. 60/048,893 filed on 06-Jun-1997, U.S. Appln. No. 60/057,661 filed on 05-Sep-1997, U.S. Appln. No. 60/048,900 filed on 06-Jun-1997, U.S. Appln. No. 60/057,662 filed on 05-Sep-1997, U.S. Appln. No. 60/048,901 filed on 06-Jun-1997, U.S. Appln. No. 60/057,646 filed on 05-Sep-1997, U.S. Appln. No. 60/048,892 filed on 06-Jun-1997,

U.S. Appln. No. 60/057,654 filed on 05-Sep-1997, U.S. Appln. No. 60/048,915 filed on 06-Jun-1997, U.S. Appln. No. 60/057,651 filed on 05-Sep-1997, U.S. Appln. No. 60/049,019 filed on 06-Jun-1997, U.S. Appln. No. 60/057,644 filed on 05-Sep-1997, U.S. Appln. No. 60/048,970 filed on 06-Jun-1997, U.S. Appln. No. 60/057,765 filed on 05-Sep-1997, U.S. Appln. No. 60/048,972 filed on 06-Jun-1997, U.S. Appln. No. 60/057,762 filed on 05-Sep-1997, U.S. Appln. No. 60/048,916 filed on 06-Jun-1997, U.S. Appln. No. 60/057,775 filed on 05-Sep-1997, U.S. Appln. No. 60/049,373 filed on 06-Jun-1997, U.S. Appln. No. 60/057,648 filed on 05-Sep-1997, U.S. Appln. No. 60/048,875 filed on 06-Jun-1997, U.S. Appln. No. 60/057,774 filed on 05-Sep-1997, U.S. Appln. No. 60/049,374 filed on 06-Jun-1997, U.S. Appln. No. 60/057,649 filed on 05-Sep-1997, U.S. Appln. No. 60/048,917 filed on 06-Jun-1997, U.S. Appln. No. 60/057,770 filed on 05-Sep-1997, U.S. Appln. No. 60/048,949 filed on 06-Jun-1997, U.S. Appln. No. 60/057,771 filed on 05-Sep-1997, U.S. Appln. No. 60/048,974 filed on 06-Jun-1997, U.S. Appln. No. 60/057,761 filed on 05-Sep-1997, U.S. Appln. No. 60/048,883 filed on 06-Jun-1997, U.S. Appln. No. 60/057,760 filed on 05-Sep-1997, U.S. Appln. No. 60/048,897 filed on 06-Jun-1997, U.S. Appln. No. 60/057,776 filed on 05-Sep-1997, U.S. Appln. No. 60/048,898 filed on 06-Jun-1997, U.S. Appln. No. 60/057,778 filed on 05-Sep-1997, U.S. Appln. No. 60/048,962 filed on 06-Jun-1997, U.S. Appln. No. 60/057,629 filed on 05-Sep-1997, U.S. Appln. No. 60/048,963 filed on 06-Jun-1997, U.S. Appln. No. 60/057,628 filed on 05-Sep-1997, U.S. Appln. No. 60/048,877 filed on 06-Jun-1997, U.S. Appln. No. 60/057,777 filed on 05-Sep-1997, U.S. Appln. No. 60/048,878 filed on 06-Jun-1997, U.S. Appln. No. 60/057,634 filed on 05-Sep-1997, U.S. Appln. No. 60/049,608 filed on 13-Jun-1997, U.S. Appln. No. 60/058,669 filed on 12-Sep-1997, U.S. Appln. No. 60/049,566 filed on 13-Jun-1997, U.S. Appln. No. 60/058,668 filed on 12-Sep-1997, U.S. Appln. No. 60/052,989 filed on 13-Jun-1997, U.S. Appln. No. 60/058,750 filed on 12-Sep-1997, U.S. Appln. No. 60/049,607 filed on 13-Jun-1997, U.S. Appln. No. 60/058,665 filed on 12-Sep-1997, U.S. Appln. No. 60/049,611 filed on 13-Jun-1997, U.S. Appln. No. 60/058,971 filed on 12-Sep-1997, U.S. Appln. No. 60/050,901 filed on 13-Jun-1997, U.S. Appln. No. 60/058,972 filed on 12-Sep-1997, U.S. Appln. No. 60/049,609 filed on 13-Jun-1997, U.S. Appln. No. 60/058,975 filed on 12-Sep-1997, U.S. Appln. No. 60/048,356 filed on 30-May-1997, U.S. Appln. No. 60/056,296 filed on 29-Aug-1997, U.S. Appln. No. 60/048,101 filed on 30-May-1997, U.S. Appln. No. 60/056,293 filed on 29-Aug-1997, U.S. Appln. No. 60/050,935 filed on 30-May-1997, U.S. Appln. No. 60/056,250 filed on 29-Aug-1997, U.S. Appln. No. 60/049,610 filed on 13-Jun-1997, U.S. Appln. No. 60/061,060 filed on 02-Oct-1997, U.S. Appln. No. 60/049,606 filed on 13-Jun-1997, U.S. Appln. No. 60/060,841 filed on 02-Oct-1997, U.S. Appln. No. 60/049,550 filed on 13-Jun-1997, U.S. Appln. No. 60/060,834 filed on 02-Oct-1997, U.S. Appln. No. 60/049,549 filed on 13-Jun-1997, U.S. Appln. No. 60/060,865 filed on 02-Oct-1997, U.S. Appln. No. 60/049,548 filed on 13-Jun-1997,

U.S. Appln. No. 60/060,844 filed on 02-Oct-1997, U.S. Appln. No. 60/049,547 filed on 13-Jun-1997, U.S. Appln. No. 60/061,059 filed on 02-Oct-1997, U.S. Appln. No. 60/051,381 filed on 01-Jul-1997, U.S. Appln. No. 60/058,598 filed on 12-Sep-1997, U.S. Appln. No. 60/051,480 filed on 01-Jul-1997, U.S. Appln. No. 60/058,663 filed on 12-Sep-1997, U.S. Appln. No. 60/051,926 filed on 08-Jul-1997, U.S. Appln. No. 60/058,785 filed on 12-Sep-1997, U.S. Appln. No. 60/052,793 filed on 08-Jul-1997, U.S. Appln. No. 60/058,664 filed on 12-Sep-1997, U.S. Appln. No. 60/051,925 filed on 08-Jul-1997, U.S. Appln. No. 60/058,660 filed on 12-Sep-1997, U.S. Appln. No. 60/051,929 filed on 08-Jul-1997, U.S. Appln. No. 60/058,661 filed on 12-Sep-1997, U.S. Appln. No. 60/052,803 filed on 08-Jul-1997, U.S. Appln. No. 60/055,722 filed on 18-Aug-1997, U.S. Appln. No. 60/052,732 filed on 08-Jul-1997, U.S. Appln. No. 60/055,723 filed on 18-Aug-1997, U.S. Appln. No. 60/051,932 filed on 08-Jul-1997, U.S. Appln. No. 60/055,948 filed on 18-Aug-1997, U.S. Appln. No. 60/051,931 filed on 08-Jul-1997, U.S. Appln. No. 60/055,949 filed on 18-Aug-1997, U.S. Appln. No. 60/051,916 filed on 08-Jul-1997, U.S. Appln. No. 60/055,953 filed on 18-Aug-1997, U.S. Appln. No. 60/051,930 filed on 08-Jul-1997, U.S. Appln. No. 60/055,950 filed on 18-Aug-1997, U.S. Appln. No. 60/051,918 filed on 08-Jul-1997, U.S. Appln. No. 60/055,947 filed on 18-Aug-1997, U.S. Appln. No. 60/051,920 filed on 08-Jul-1997, U.S. Appln. No. 60/055,964 filed on 18-Aug-1997, U.S. Appln. No. 60/052,733 filed on 08-Jul-1997, U.S. Appln. No. 60/056,360 filed on 18-Aug-1997, U.S. Appln. No. 60/052,795 filed on 08-Jul-1997, U.S. Appln. No. 60/055,684 filed on 18-Aug-1997, U.S. Appln. No. 60/051,919 filed on 08-Jul-1997, U.S. Appln. No. 60/055,984 filed on 18-Aug-1997, U.S. Appln. No. 60/051,928 filed on 08-Jul-1997, U.S. Appln. No. 60/055,954 filed on 18-Aug-1997, U.S. Appln. No. 60/052,870 filed on 16-Jul-1997, U.S. Appln. No. 60/055,952 filed on 18-Aug-1997, U.S. Appln. No. 60/052,871 filed on 16-Jul-1997, U.S. Appln. No. 60/055,725 filed on 18-Aug-1997, U.S. Appln. No. 60/052,872 filed on 16-Jul-1997, U.S. Appln. No. 60/056,359 filed on 18-Aug-1997, U.S. Appln. No. 60/052,661 filed on 16-Jul-1997, U.S. Appln. No. 60/055,985 filed on 18-Aug-1997, U.S. Appln. No. 60/052,874 filed on 16-Jul-1997, U.S. Appln. No. 60/055,724 filed on 18-Aug-1997, U.S. Appln. No. 60/052,873 filed on 16-Jul-1997, U.S. Appln. No. 60/055,726 filed on 18-Aug-1997, U.S. Appln. No. 60/052,875 filed on 16-Jul-1997, U.S. Appln. No. 60/056,361 filed on 18-Aug-1997, U.S. Appln. No. 60/053,440 filed on 22-Jul-1997, U.S. Appln. No. 60/055,989 filed on 18-Aug-1997, U.S. Appln. No. 60/053,441 filed on 22-Jul-1997, U.S. Appln. No. 60/055,946 filed on 18-Aug-1997, U.S. Appln. No. 60/053,442 filed on 22-Jul-1997, U.S. Appln. No. 60/055,683 filed on 18-Aug-1997, U.S. Appln. No. 60/054,212 filed on 30-Jul-1997, U.S. Appln. No. 60/055,968 filed on 18-Aug-1997, U.S. Appln. No. 60/054,209 filed on 30-Jul-1997, U.S. Appln. No. 60/055,972 filed on 18-Aug-1997, U.S. Appln. No. 60/054,234 filed on 30-Jul-1997, U.S. Appln. No. 60/055,969 filed on 18-Aug-1997, U.S. Appln. No. 60/055,386 filed on 05-Aug-1997, U.S.

Appln. No. 60/055,986 filed on 18-Aug-1997, U.S. Appln. No. 60/054,807 filed on 05-Aug-1997, U.S. Appln. No. 60/055,970 filed on 18-Aug-1997, U.S. Appln. No. 60/054,215 filed on 30-Jul-1997, U.S. Appln. No. 60/056,543 filed on 19-Aug-1997, U.S. Appln. No. 60/054,218 filed on 30-Jul-1997, U.S. Appln. No. 60/056,561 filed on 19-Aug-1997, U.S. Appln. No. 60/054,214 filed on 30-Jul-1997, U.S. Appln. No. 60/056,534 filed on 19-Aug-1997, U.S. Appln. No. 60/054,236 filed on 30-Jul-1997, U.S. Appln. No. 60/056,729 filed on 19-Aug-1997, U.S. Appln. No. 60/054,213 filed on 30-Jul-1997, U.S. Appln. No. 60/056,727 filed on 19-Aug-1997, U.S. Appln. No. 60/054,211 filed on 30-Jul-1997, U.S. Appln. No. 60/056,554 filed on 19-Aug-1997, U.S. Appln. No. 60/054,217 filed on 30-Jul-1997, U.S. Appln. No. 60/056,730 filed on 19-Aug-1997, U.S. Appln. No. 60/055,312 filed on 05-Aug-1997, U.S. Appln. No. 60/056,563 filed on 19-Aug-1997, U.S. Appln. No. 60/055,309 filed on 05-Aug-1997, U.S. Appln. No. 60/056,557 filed on 19-Aug-1997, U.S. Appln. No. 60/055,310 filed on 05-Aug-1997, U.S. Appln. No. 60/056,371 filed on 19-Aug-1997, U.S. Appln. No. 60/054,798 filed on 05-Aug-1997, U.S. Appln. No. 60/056,732 filed on 19-Aug-1997, U.S. Appln. No. 60/056,369 filed on 19-Aug-1997, U.S. Appln. No. 60/056,535 filed on 19-Aug-1997, U.S. Appln. No. 60/056,556 filed on 19-Aug-1997, U.S. Appln. No. 60/056,555 filed on 19-Aug-1997, U.S. Appln. No. 60/054,806 filed on 05-Aug-1997, U.S. Appln. No. 60/056,366 filed on 19-Aug-1997, U.S. Appln. No. 60/054,809 filed on 05-Aug-1997, U.S. Appln. No. 60/056,364 filed on 19-Aug-1997, U.S. Appln. No. 60/054,804 filed on 05-Aug-1997, U.S. Appln. No. 60/056,370 filed on 19-Aug-1997, U.S. Appln. No. 60/054,803 filed on 05-Aug-1997, U.S. Appln. No. 60/056,731 filed on 19-Aug-1997, U.S. Appln. No. 60/055,311 filed on 05-Aug-1997, U.S. Appln. No. 60/056,365 filed on 19-Aug-1997, U.S. Appln. No. 60/054,808 filed on 05-Aug-1997, U.S. Appln. No. 60/056,367 filed on 19-Aug-1997, U.S. Appln. No. 60/056,726 filed on 19-Aug-1997, U.S. Appln. No. 60/056,368 filed on 19-Aug-1997, U.S. Appln. No. 60/056,728 filed on 19-Aug-1997, U.S. Appln. No. 60/056,628 filed on 19-Aug-1997, U.S. Appln. No. 60/056,629 filed on 19-Aug-1997, U.S. Appln. No. 60/056,270 filed on 29-Aug-1997, U.S. Appln. No. 60/056,271 filed on 29-Aug-1997, U.S. Appln. No. 60/056,247 filed on 29-Aug-1997, U.S. Appln. No. 60/056,073 filed on 29-Aug-1997, U.S. Appln. No. 60/057,669 filed on 05-Sep-1997, U.S. Appln. No. 60/057,663 filed on 05-Sep-1997, U.S. Appln. No. 60/057,626 filed on 05-Sep-1997, U.S. Appln. No. 60/058,666 filed on 12-Sep-1997, U.S. Appln. No. 60/058,973 filed on 12-Sep-1997, U.S. Appln. No. 60/058,974 filed on 12-Sep-1997, U.S. Appln. No. 60/058,667 filed on 12-Sep-1997, U.S. Appln. No. 60/060,837 filed on 02-Oct-1997, U.S. Appln. No. 60/060,862 filed on 02-Oct-1997, U.S. Appln. No. 60/060,839 filed on 02-Oct-1997, U.S. Appln. No. 60/060,866 filed on 02-Oct-1997, U.S. Appln. No. 60/060,843 filed on 02-Oct-1997, U.S. Appln. No. 60/060,836 filed on 02-Oct-1997, U.S. Appln. No. 60/060,838 filed on 02-Oct-1997, U.S. Appln. No. 60/060,874 filed on 02-Oct-1997, U.S. Appln. No. 60/060,833 filed on 02-Oct-1997,

U.S. Appln. No. 60/060,884 filed on 02-Oct-1997, U.S. Appln. No. 60/060,880 filed on 02-Oct-1997, U.S. Appln. No. 60/061,463 filed on 09-Oct-1997, U.S. Appln. No. 60/061,529 filed on 09-Oct-1997, U.S. Appln. No. 60/071,498 filed on 09-Oct-1997, U.S. Appln. No. 60/061,527 filed on 09-Oct-1997, U.S. Appln. No. 60/061,536 filed on 09-Oct-1997, U.S. Appln. No. 60/061,532 filed on 09-Oct-1997, U.S. Appln. No. 60/063,099 filed on 24-Oct-1997, U.S. Appln. No. 60/063,088
5 filed on 24-Oct-1997, U.S. Appln. No. 60/063,100 filed on 24-Oct-1997, U.S. Appln. No. 60/063,387 filed on 24-Oct-1997, U.S. Appln. No. 60/063,148 filed on 24-Oct-1997, U.S. Appln. No. 60/063,386 filed on 24-Oct-1997, U.S. Appln. No. 60/062,784 filed on 24-Oct-1997, U.S. Appln. No. 60/063,091 filed on 24-Oct-1997, U.S. Appln. No. 60/063,090 filed on 24-Oct-1997,
10 U.S. Appln. No. 60/063,089 filed on 24-Oct-1997, U.S. Appln. No. 60/063,092 filed on 24-Oct-1997, U.S. Appln. No. 60/063,111 filed on 24-Oct-1997, U.S. Appln. No. 60/063,101 filed on 24-Oct-1997, U.S. Appln. No. 60/063,109 filed on 24-Oct-1997, U.S. Appln. No. 60/063,110 filed on 24-Oct-1997, U.S. Appln. No. 60/063,098 filed on 24-Oct-1997, U.S. Appln. No. 60/063,097 filed on 24-Oct-1997, U.S. Appln. No. 60/064,911 filed on 07-Nov-1997, U.S. Appln. No. 60/064,912
15 filed on 07-Nov-1997, U.S. Appln. No. 60/064,983 filed on 07-Nov-1997, U.S. Appln. No. 60/064,900 filed on 07-Nov-1997, U.S. Appln. No. 60/064,988 filed on 07-Nov-1997, U.S. Appln. No. 60/064,987 filed on 07-Nov-1997, U.S. Appln. No. 60/064,908 filed on 07-Nov-1997, U.S. Appln. No. 60/064,984 filed on 07-Nov-1997, U.S. Appln. No. 60/064,985 filed on 07-Nov-1997, U.S. Appln. No. 60/066,094 filed on 17-Nov-1997, U.S. Appln. No. 60/066,100 filed on 17-Nov-
20 1997, U.S. Appln. No. 60/066,089 filed on 17-Nov-1997, U.S. Appln. No. 60/066,095 filed on 17-Nov-1997, U.S. Appln. No. 60/066,090 filed on 17-Nov-1997, U.S. Appln. No. 60/068,006 filed on 18-Dec-1997, U.S. Appln. No. 60/068,057 filed on 18-Dec-1997, U.S. Appln. No. 60/068,007 filed on 18-Dec-1997, U.S. Appln. No. 60/068,008 filed on 18-Dec-1997, U.S. Appln. No. 60/068,054 filed on 18-Dec-1997, U.S. Appln. No. 60/068,064 filed on 18-Dec-1997, U.S. Appln.
25 No. 60/068,053 filed on 18-Dec-1997, U.S. Appln. No. 60/070,923 filed on 18-Dec-1997, U.S. Appln. No. 60/068,365 filed on 19-Dec-1997, U.S. Appln. No. 60/068,169 filed on 19-Dec-1997, U.S. Appln. No. 60/068,367 filed on 19-Dec-1997, U.S. Appln. No. 60/068,369 filed on 19-Dec-1997, U.S. Appln. No. 60/068,368 filed on 19-Dec-1997, U.S. Appln. No. 60/070,657 filed on 07-Jan-1998, U.S. Appln. No. 60/070,692 filed on 07-Jan-1998, U.S. Appln. No. 60/070,704 filed on
30 07-Jan-1998, U.S. Appln. No. 60/070,658 filed on 07-Jan-1998, U.S. Appln. No. 60/073,160 filed on 30-Jan-1998, U.S. Appln. No. 60/073,159 filed on 30-Jan-1998, U.S. Appln. No. 60/073,165 filed on 30-Jan-1998, U.S. Appln. No. 60/073,164 filed on 30-Jan-1998, U.S. Appln. No. 60/073,167 filed on 30-Jan-1998, U.S. Appln. No. 60/073,162 filed on 30-Jan-1998, U.S. Appln. No. 60/073,161 filed on 30-Jan-1998, U.S. Appln. No. 60/073,170 filed on 30-Jan-1998, U.S.
35 Appln. No. 60/074,141 filed on 09-Feb-1998, U.S. Appln. No. 60/074,341 filed on 09-Feb-1998,

U.S. Appln. No. 60/074,037 filed on 09-Feb-1998, U.S. Appln. No. 60/074,157 filed on 09-Feb-1998, U.S. Appln. No. 60/074,118 filed on 09-Feb-1998, U.S. Appln. No. 60/076,051 filed on 26-Feb-1998, U.S. Appln. No. 60/076,053 filed on 26-Feb-1998, U.S. Appln. No. 60/076,054 filed on 26-Feb-1998, U.S. Appln. No. 60/076,052 filed on 26-Feb-1998, U.S. Appln. No. 60/076,057 filed on 26-Feb-1998, U.S. Appln. No. 60/077,714 filed on 12-Mar-1998, U.S. Appln. No. 60/077,687 filed on 12-Mar-1998, U.S. Appln. No. 60/077,686 filed on 12-Mar-1998, U.S. Appln. No. 60/077,696 filed on 12-Mar-1998, U.S. Appln. No. 60/078,566 filed on 19-Mar-1998, U.S. Appln. No. 60/078,574 filed on 19-Mar-1998, U.S. Appln. No. 60/078,576 filed on 19-Mar-1998, U.S. Appln. No. 60/078,579 filed on 19-Mar-1998, U.S. Appln. No. 60/078,563 filed on 19-Mar-1998, U.S. Appln. No. 60/078,573 filed on 19-Mar-1998, U.S. Appln. No. 60/078,578 filed on 19-Mar-1998, U.S. Appln. No. 60/078,581 filed on 19-Mar-1998, U.S. Appln. No. 60/078,577 filed on 19-Mar-1998, U.S. Appln. No. 60/080,314 filed on 01-Apr-1998, U.S. Appln. No. 60/080,312 filed on 01-Apr-1998, U.S. Appln. No. 60/080,313 filed on 01-Apr-1998, U.S. Appln. No. 60/085,180 filed on 12-May-1998, U.S. Appln. No. 60/085,105 filed on 12-May-1998, U.S. Appln. No. 60/085,094 filed on 12-May-1998, U.S. Appln. No. 60/085,093 filed on 12-May-1998, U.S. Appln. No. 60/085,924 filed on 18-May-1998, U.S. Appln. No. 60/085,906 filed on 18-May-1998, U.S. Appln. No. 60/085,927 filed on 18-May-1998, U.S. Appln. No. 60/085,920 filed on 18-May-1998, U.S. Appln. No. 60/085,928 filed on 18-May-1998, U.S. Appln. No. 60/085,925 filed on 18-May-1998, U.S. Appln. No. 60/085,921 filed on 18-May-1998, U.S. Appln. No. 60/085,923 filed on 18-May-1998, U.S. Appln. No. 60/085,922 filed on 18-May-1998, U.S. Appln. No. 60/090,112 filed on 22-Jun-1998, U.S. Appln. No. 60/089,508 filed on 16-Jun-1998, U.S. Appln. No. 60/089,507 filed on 16-Jun-1998, U.S. Appln. No. 60/089,510 filed on 16-Jun-1998, U.S. Appln. No. 60/089,509 filed on 16-Jun-1998, U.S. Appln. No. 60/090,113 filed on 22-Jun-1998, U.S. Appln. No. 60/092,956 filed on 15-Jul-1998, U.S. Appln. No. 60/092,921 filed on 15-Jul-1998, U.S. Appln. No. 60/092,922 filed on 15-Jul-1998, U.S. Appln. No. 60/094,657 filed on 30-Jul-1998, U.S. Appln. No. 60/095,486 filed on 05-Aug-1998, U.S. Appln. No. 60/096,319 filed on 12-Aug-1998, U.S. Appln. No. 60/095,455 filed on 06-Aug-1998, U.S. Appln. No. 60/095,454 filed on 06-Aug-1998, U.S. Appln. No. 60/097,917 filed on 25-Aug-1998, U.S. Appln. No. 60/098,634 filed on 31-Aug-1998, U.S. Appln. No. 60/101,546 filed on 23-Sep-1998, U.S. Appln. No. 60/102,895 filed on 02-Oct-1998, U.S. Appln. No. 60/108,207 filed on 12-Nov-1998, U.S. Appln. No. 60/113,006 filed on 18-Dec-1998, U.S. Appln. No. 60/112,809 filed on 17-Dec-1998, U.S. Appln. No. 60/116,330 filed on 19-Jan-1999, U.S. Appln. No. 60/119,468 filed on 10-Feb-1999, U.S. Appln. No. 60/125,055 filed on 18-Mar-1999, U.S. Appln. No. 60/128,693 filed on 09-Apr-1999, U.S. Appln. No. 60/130,991 filed on 26-Apr-1999, U.S. Appln. No. 60/137,725 filed on 07-Jun-1999, U.S. Appln. No. 60/145,220 filed on 23-Jul-1999, U.S. Appln. No. 60/149,182 filed on 17-

Aug-1999, U.S. Appln. No. 60/152,317 filed on 03-Sep-1999, U.S. Appln. No. 60/152,315 filed on 03-Sep-1999, U.S. Appln. No. 60/155,709 filed on 24-Sep-1999, U.S. Appln. No. 60/163,085 filed on 02-Nov-1999, U.S. Appln. No. 60/172,411 filed on 17-Dec-1999, U.S. Appln. No. 60/162,239 filed on 29-Oct-1999, U.S. Appln. No. 60/215,139 filed on 30-Jun-2000, U.S. Appln. No. 5 60/162,211 filed on 29-Oct-1999, U.S. Appln. No. 60/215,138 filed on 30-Jun-2000, U.S. Appln. No. 60/162,240 filed on 29-Oct-1999, U.S. Appln. No. 60/215,131 filed on 30-Jun-2000, U.S. Appln. No. 60/162,237 filed on 29-Oct-1999, U.S. Appln. No. 60/219,666 filed on 21-Jul-2000, U.S. Appln. No. 60/162,238 filed on 29-Oct-1999, U.S. Appln. No. 60/215,134 filed on 30-Jun-2000, U.S. Appln. No. 60/163,580 filed on 05-Nov-1999, U.S. Appln. No. 60/215,130 filed on 30-10 Jun-2000, U.S. Appln. No. 60/163,577 filed on 05-Nov-1999, U.S. Appln. No. 60/215,137 filed on 30-Jun-2000, U.S. Appln. No. 60/163,581 filed on 05-Nov-1999, U.S. Appln. No. 60/215,133 filed on 30-Jun-2000, U.S. Appln. No. 60/163,576 filed on 05-Nov-1999, U.S. Appln. No. 60/221,366 filed on 27-Jul-2000, U.S. Appln. No. 60/164,344 filed on 09-Nov-1999, U.S. Appln. No. 60/195,296 filed on 07-Apr-2000, U.S. Appln. No. 60/221,367 filed on 27-Jul-2000, U.S. Appln. 15 No. 60/164,835 filed on 12-Nov-1999, U.S. Appln. No. 60/221,142 filed on 27-Jul-2000, U.S. Appln. No. 60/164,744 filed on 12-Nov-1999, U.S. Appln. No. 60/215,140 filed on 30-Jun-2000, U.S. Appln. No. 60/164,735 filed on 12-Nov-1999, U.S. Appln. No. 60/221,193 filed on 27-Jul-2000, U.S. Appln. No. 60/164,825 filed on 12-Nov-1999, U.S. Appln. No. 60/222,904 filed on 03-Aug-2000, U.S. Appln. No. 60/164,834 filed on 12-Nov-1999, U.S. Appln. No. 60/224,007 filed 20 on 04-Aug-2000, U.S. Appln. No. 60/164,750 filed on 12-Nov-1999, U.S. Appln. No. 60/215,128 filed on 30-Jun-2000, U.S. Appln. No. 60/166,415 filed on 19-Nov-1999, U.S. Appln. No. 60/215,136 filed on 30-Jun-2000, U.S. Appln. No. 60/166,414 filed on 19-Nov-1999, U.S. Appln. No. 60/219,665 filed on 21-Jul-2000, U.S. Appln. No. 60/164,731 filed on 12-Nov-1999, U.S. Appln. No. 60/215,132 filed on 30-Jun-2000, U.S. Appln. No. 60/226,280 filed on 18-Aug-2000, 25 U.S. Appln. No. 60/256,968 filed on 21-Dec-2000, U.S. Appln. No. 60/226,380 filed on 18-Aug-2000, U.S. Appln. No. 60/259,803 filed on 05-Jan-2001, U.S. Appln. No. 60/228,084 filed on 28-Aug-2000, U.S. Appln. No. 09/915,582 filed on 27-Jul-2001, U.S. Appln. No. 60/231,968 filed on 12-Sep-2000, U.S. Appln. No. 60/236,326 filed on 29-Sep-2000, U.S. Appln. No. 60/234,211 filed on 20-Sep-2000, U.S. Appln. No. 60/226,282 filed on 18-Aug-2000, U.S. Appln. No. 60/232,104 30 filed on 12-Sep-2000, U.S. Appln. No. 60/234,210 filed on 20-Sep-2000, U.S. Appln. No. 60/226,278 filed on 18-Aug-2000, U.S. Appln. No. 60/259,805 filed on 05-Jan-2001, U.S. Appln. No. 60/226,279 filed on 18-Aug-2000, U.S. Appln. No. 60/259,678 filed on 05-Jan-2001, U.S. Appln. No. 60/226,281 filed on 18-Aug-2000, U.S. Appln. No. 60/231,969 filed on 12-Sep-2000, U.S. Appln. No. 60/228,086 filed on 28-Aug-2000, U.S. Appln. No. 60/259,516 filed on 04-Jan-35 2001, U.S. Appln. No. 60/228,083 filed on 28-Aug-2000, U.S. Appln. No. 60/259,804 filed on 05-

Jan-2001, U.S. Appln. No. 60/270,658 filed on 23-Feb-2001, U.S. Appln. No. 60/304,444 filed on 12-Jul-2001, U.S. Appln. No. 60/270,625 filed on 23-Feb-2001, U.S. Appln. No. 60/304,417 filed on 12-Jul-2001, U.S. Appln. No. 60/295,869 filed on 06-Jun-2001, U.S. Appln. No. 60/304,121 filed on 11-Jul-2001, U.S. Appln. No. 60/311,085 filed on 10-Aug-2001, U.S. Appln. No. 5 60/325,209 filed on 28-Sep-2001, U.S. Appln. No. 60/330,629 filed on 26-Oct-2001, U.S. Appln. No. 60/331,046 filed on 07-Nov-2001, U.S. Appln. No. 60/358,554 filed on 22-Feb-2002, U.S. Appln. No. 60/358,714 filed on 25-Feb-2002, U.S. Appln. No. 60/277,340 filed on 21-Mar-2001, U.S. Appln. No. 60/306,171 filed on 19-Jul-2001, U.S. Appln. No. 60/278,650 filed on 27-Mar-2001, U.S. Appln. No. 60/331,287 filed on 13-Nov-2001, U.S. Appln. No. 09/950,082 filed on 12- 10 Sep-2001, U.S. Appln. No. 09/950,083 filed on 12-Sep-2001, PCT Appln. No. US00/29363 filed on 25-Oct-2000, PCT Appln. No. US00/29360 filed on 25-Oct-2000, PCT Appln. No. US00/29362 filed on 25-Oct-2000, PCT Appln. No. US00/29365 filed on 25-Oct-2000, PCT Appln. No. US00/29364 filed on 25-Oct-2000, PCT Appln. No. US00/30040 filed on 01-Nov-2000, PCT Appln. No. US00/30037 filed on 01-Nov-2000, PCT Appln. No. US00/30045 filed on 15 01-Nov-2000, PCT Appln. No. US00/30036 filed on 01-Nov-2000, PCT Appln. No. US00/30039 filed on 01-Nov-2000, PCT Appln. No. US00/30654 filed on 08-Nov-2000, PCT Appln. No. US00/30628 filed on 08-Nov-2000, PCT Appln. No. US00/30653 filed on 08-Nov-2000, PCT Appln. No. US00/30629 filed on 08-Nov-2000, PCT Appln. No. US00/30679 filed on 08-Nov-2000, PCT Appln. No. US00/30674 filed on 08-Nov-2000, PCT Appln. No. US00/31162 filed on 20 15-Nov-2000, PCT Appln. No. US00/31282 filed on 15-Nov-2000, PCT Appln. No. US00/30657 filed on 08-Nov-2000, PCT Appln. No. US01/01396 filed on 17-Jan-2001, PCT Appln. No. US01/01387 filed on 17-Jan-2001, PCT Appln. No. US01/01567 filed on 17-Jan-2001, PCT Appln. No. US01/01431 filed on 17-Jan-2001, PCT Appln. No. US01/01432 filed on 17-Jan-2001, PCT Appln. No. US01/00544 filed on 09-Jan-2001, PCT Appln. No. US01/01435 filed on 17-Jan- 25 2001, PCT Appln. No. US01/01386 filed on 17-Jan-2001, PCT Appln. No. US01/01565 filed on 17-Jan-2001, PCT Appln. No. US01/01394 filed on 17-Jan-2001, PCT Appln. No. US01/01434 filed on 17-Jan-2001, PCT Appln. No. US01/01397 filed on 17-Jan-2001, PCT Appln. No. US01/01385 filed on 17-Jan-2001, PCT Appln. No. US01/01384 filed on 17-Jan-2001, PCT Appln. No. US01/01383 filed on 17-Jan-2001, PCT Appln. No. (Atty. Dkt. No. PS735; 30 unassigned) filed on 21-Feb-2002, PCT Appln. No. (Atty. Dkt. No. PS736; unassigned) filed on 21-Feb-2002, U.S. Appln. No. 09/148,545 filed on 04-Sep-1998, U.S. Appln. No. 09/621,011 filed on 20-Jul-2000, U.S. Appln. No. 09/981,876 filed on 19-Oct-2001, U.S. Appln. No. 09/149,476 filed on 08-Sep-1998, U.S. Appln. No. 09/809,391 filed on 16-Mar-2001, U.S. Appln. No. 09/882,171 filed on 18-Jun-2001, U.S. Appln. No. 60/190,068 filed on 17-Mar-2000, U.S. Appln. 35 No. 09/152,060 filed on 11-Sep-1998, U.S. Appln. No. 09/852,797 filed on 11-May-2001, U.S.

Appln. No. 09/853,161 filed on 11-May-2001, U.S. Appln. No. 09/852,659 filed on 11-May-2001, U.S. Appln. No. 10/058,993 filed on 30-Jan-2002, U.S. Appln. No. 60/265,583 filed on 02-Feb-2001, U.S. Appln. No. 09/154,707 filed on 17-Sep-1998, U.S. Appln. No. 09/966,262 filed on 01-Oct-2001, U.S. Appln. No. 09/983,966 filed on 26-Oct-2001, U.S. Appln. No. 10/059,395 filed on 5 31-Jan-2002, U.S. Appln. No. 09/984,245 filed on 29-Oct-2001, U.S. Appln. No. 09/166,780 filed on 06-Oct-1998, U.S. Appln. No. 09/577,145 filed on 24-May-2000, U.S. Appln. No. 09/814,122 filed on 22-Mar-2001, U.S. Appln. No. 09/189,144 filed on 10-Nov-1998, U.S. Appln. No. 09/690,454 filed on 18-Oct-2000, U.S. Appln. No. (Atty. Dkt. No. PZ006G13A; unassigned) filed on 05-Feb-2002, U.S. Appln. No. 10/062,599 filed on 05-Feb-2002, U.S. Appln. No. 09/205,258 10 filed on 04-Dec-1998, U.S. Appln. No. 09/933,767 filed on 22-Aug-2001, U.S. Appln. No. 60/184,836 filed on 24-Feb-2000, U.S. Appln. No. 60/193,170 filed on 29-Mar-2000, U.S. Appln. No. 10/023,282 filed on 20-Dec-2001, U.S. Appln. No. 10/004,860 filed on 07-Dec-2001, U.S. Appln. No. 09/209,462 filed on 11-Dec-1998, U.S. Appln. No. 09/213,365 filed on 17-Dec-1998, U.S. Appln. No. 09/627,081 filed on 27-Jul-2000, U.S. Appln. No. 09/227,357 filed on 08-Jan- 15 1999, U.S. Appln. No. 09/983,802 filed on 25-Oct-2001, U.S. Appln. No. 09/973,278 filed on 10-Oct-2001, U.S. Appln. No. 60/239,899 filed on 13-Oct-2000, U.S. Appln. No. 09/984,490 filed on 30-Oct-2001, U.S. Appln. No. 09/776,724 filed on 06-Feb-2001, U.S. Appln. No. 09/229,982 filed on 14-Jan-1999, U.S. Appln. No. 09/669,688 filed on 26-Sep-2000, U.S. Appln. No. 60/180,909 filed on 08-Feb-2000, U.S. Appln. No. 09/236,557 filed on 26-Jan-1999, U.S. Appln. No. 20 09/666,984 filed on 21-Sep-2000, U.S. Appln. No. 09/820,649 filed on 30-Mar-2001, U.S. Appln. No. 60/295,558 filed on 05-Jun-2001, U.S. Appln. No. 09/244,112 filed on 04-Feb-1999, U.S. Appln. No. 09/774,639 filed on 01-Feb-2001, U.S. Appln. No. 09/969,730 filed on 04-Oct-2001, U.S. Appln. No. 60/238,291 filed on 06-Oct-2000, U.S. Appln. No. 09/251,329 filed on 17-Feb-1999, U.S. Appln. No. 09/716,128 filed on 17-Nov-2000, U.S. Appln. No. 09/257,179 filed on 25- 25 Feb-1999, U.S. Appln. No. 09/729,835 filed on 06-Dec-2000, U.S. Appln. No. 09/262,109 filed on 04-Mar-1999, U.S. Appln. No. 09/722,329 filed on 28-Nov-2000, U.S. Appln. No. (Atty. Dkt. No. PZ016P1C1; unassigned) filed on 17-Jan-2002, U.S. Appln. No. 60/262,066 filed on 18-Jan-2001, U.S. Appln. No. 09/281,976 filed on 31-Mar-1999, U.S. Appln. No. 09/288,143 filed on 08-Apr-1999, U.S. Appln. No. 09/984,429 filed on 30-Oct-2001, U.S. Appln. No. 60/244,591 filed on 01- 30 Nov-2000, U.S. Appln. No. 09/296,622 filed on 23-Apr-1999, U.S. Appln. No. 09/305,736 filed on 05-May-1999, U.S. Appln. No. 09/818,683 filed on 28-Mar-2001, U.S. Appln. No. 09/974,879 filed on 12-Oct-2001, U.S. Appln. No. 60/239,893 filed on 13-Oct-2000, U.S. Appln. No. 09/334,595 filed on 17-Jun-1999, U.S. Appln. No. 09/348,457 filed on 07-Jul-1999, U.S. Appln. No. 09/739,907 filed on 20-Dec-2000, U.S. Appln. No. 09/938,671 filed on 27-Aug-2001, U.S. 35 Appln. No. 09/363,044 filed on 29-Jul-1999, U.S. Appln. No. 09/813,153 filed on 21-Mar-2001,

U.S. Appln. No. 09/949,925 filed on 12-Sep-2001, U.S. Appln. No. 60/232,150 filed on 12-Sep-2000, U.S. Appln. No. 09/369,247 filed on 05-Aug-1999, U.S. Appln. No. 10/062,548 filed on 05-Feb-2002, U.S. Appln. No. 09/382,572 filed on 25-Aug-1999, U.S. Appln. No. 09/716,129 filed on 17-Nov-2000, U.S. Appln. No. 09/393,022 filed on 09-Sep-1999, U.S. Appln. No. 09/798,889
5 filed on 06-Mar-2001, U.S. Appln. No. 09/397,945 filed on 17-Sep-1999, U.S. Appln. No. 09/437,658 filed on 10-Nov-1999, U.S. Appln. No. 09/892,877 filed on 28-Jun-2001, U.S. Appln. No. 09/948,783 filed on 10-Sep-2001, U.S. Appln. No. 60/231,846 filed on 11-Sep-2000, U.S. Appln. No. 09/461,325 filed on 14-Dec-1999, U.S. Appln. No. 10/050,873 filed on 18-Jan-2002, U.S. Appln. No. 60/263,230 filed on 23-Jan-2001, U.S. Appln. No. 60/263,681 filed on 24-Jan-
10 2001, U.S. Appln. No. 10/012,542 filed on 12-Dec-2001, U.S. Appln. No. 09/482,273 filed on 13-Jan-2000, U.S. Appln. No. 60/234,925 filed on 25-Sep-2000, U.S. Appln. No. 09/984,276 filed on 29-Oct-2001, U.S. Appln. No. 09/984,271 filed on 29-Oct-2001, U.S. Appln. No. 09/489,847 filed on 24-Jan-2000, U.S. Appln. No. 60/350,898 filed on 25-Jan-2002, U.S. Appln. No. 09/511,554 filed on 23-Feb-2000, U.S. Appln. No. 09/739,254 filed on 19-Dec-2000, U.S. Appln. No.
15 09/904,615 filed on 16-Jul-2001, U.S. Appln. No. 10/054,988 filed on 25-Jan-2002, U.S. Appln. No. 09/531,119 filed on 20-Mar-2000, U.S. Appln. No. 09/820,893 filed on 30-Mar-2001, U.S. Appln. No. 09/565,391 filed on 05-May-2000, U.S. Appln. No. 09/948,820 filed on 10-Sep-2001, U.S. Appln. No. 09/591,316 filed on 09-Jun-2000, U.S. Appln. No. 09/895,298 filed on 02-Jul-2001, U.S. Appln. No. 09/618,150 filed on 17-Jul-2000, U.S. Appln. No. 09/985,153 filed on 01-
20 Nov-2001, U.S. Appln. No. 09/628,508 filed on 28-Jul-2000, U.S. Appln. No. 09/997,131 filed on 30-Nov-2001, U.S. Appln. No. 09/661,453 filed on 13-Sep-2000, U.S. Appln. No. 10/050,882 filed on 18-Jan-2002, U.S. Appln. No. 09/684,524 filed on 10-Oct-2000, U.S. Appln. No. 10/050,704 filed on 18-Jan-2002, U.S. Appln. No. 09/726,643 filed on 01-Dec-2000, U.S. Appln. No. 10/042,141 filed on 11-Jan-2002, U.S. Appln. No. 09/756,168 filed on 09-Jan-2001, U.S.
25 Appln. No. 09/781,417 filed on 13-Feb-2001, U.S. Appln. No. (Atty. Dkt. No. PZ042PIC1; unassigned) filed on 01-Feb-2002, U.S. Appln. No. 09/789,561 filed on 22-Feb-2001, U.S. Appln. No. 09/800,729 filed on 08-Mar-2001, U.S. Appln. No. 09/832,129 filed on 11-Apr-2001, PCT Appln. No.US98/04482 filed on 06-Mar-1998, PCT Appln. No.US98/04493 filed on 06-Mar-1998, PCT Appln. No.US98/04858 filed on 12-Mar-1998, PCT Appln. No.US98/05311 filed on 19-Mar-
30 1998, PCT Appln. No.US98/06801 filed on 07-Apr-1998, PCT Appln. No.US98/10868 filed on 28-May-1998, PCT Appln. No.US98/11422 filed on 04-Jun-1998, PCT Appln. No.US01/05614 filed on 21-Feb-2001, PCT Appln. No.US98/12125 filed on 11-Jun-1998, PCT Appln. No.US98/13608 filed on 30-Jun-1998, PCT Appln. No.US98/13684 filed on 07-Jul-1998, PCT Appln. No.US98/14613 filed on 15-Jul-1998, PCT Appln. No.US98/15949 filed on 29-Jul-1998,
35 PCT Appln. No.US98/16235 filed on 04-Aug-1998, PCT Appln. No.US98/17044 filed on 18-Aug-

1998, PCT Appln. No.US98/17709 filed on 27-Aug-1998, PCT Appln. No.US98/18360 filed on 03-Sep-1998, PCT Appln. No.(Atty. Dkt. No. PZ016PCT2; unassigned) filed on 17-Jan-2002, PCT Appln. No.US98/20775 filed on 01-Oct-1998, PCT Appln. No.US98/21142 filed on 08-Oct-1998, PCT Appln. No.US98/22376 filed on 23-Oct-1998, PCT Appln. No.US98/23435 filed on 5 04-Nov-1998, PCT Appln. No.US98/27059 filed on 17-Dec-1998, PCT Appln. No.US99/00108 filed on 06-Jan-1999, PCT Appln. No.US99/01621 filed on 27-Jan-1999, PCT Appln. No.US99/02293 filed on 04-Feb-1999, PCT Appln. No.US99/03939 filed on 24-Feb-1999, PCT Appln. No.US99/05721 filed on 11-Mar-1999, PCT Appln. No.US99/05804 filed on 18-Mar-1999, PCT Appln. No.US99/09847 filed on 06-May-1999, PCT Appln. No.US99/13418 filed on 15-Jun-10 1999, PCT Appln. No.US99/15849 filed on 14-Jul-1999, PCT Appln. No.US01/00911 filed on 12-Jan-2001, PCT Appln. No.US01/29871 filed on 24-Sep-2001, PCT Appln. No.US99/17130 filed on 29-Jul-1999, PCT Appln. No.US99/19330 filed on 24-Aug-1999, PCT Appln. No.US99/22012 filed on 22-Sep-1999, PCT Appln. No.US99/26409 filed on 09-Nov-1999, PCT Appln. No.US99/29950 filed on 16-Dec-1999, PCT Appln. No.US00/00903 filed on 18-Jan-2000, PCT 15 Appln. No.US00/03062 filed on 08-Feb-2000, PCT Appln. No.US00/06783 filed on 16-Mar-2000, PCT Appln. No.US00/08979 filed on 06-Apr-2000, PCT Appln. No.US00/15187 filed on 02-Jun-2000, PCT Appln. No.US00/19735 filed on 20-Jul-2000, PCT Appln. No.US00/22325 filed on 16-Aug-2000, PCT Appln. No.US00/24008 filed on 31-Aug-2000, PCT Appln. No.US00/26013 filed on 22-Sep-2000, PCT Appln. No.US00/28664 filed on 17-Oct-2000, US Appln. No. 09/833,245 20 filed on 12-Apr-2001, and PCT Appln. No. US01/11988 filed on 12-Apr-2001.

Applicant's File	International Application
Reference Number: PS904PCT	Number: Unassigned

INDICATIONS RELATING TO DEPOSITED BIOLOGICAL MATERIAL

(PCT Rule 13bis)

A. The indications made below relate to the deposited biological material referred to in Table 1A of the description.

B. IDENTIFICATION OF DEPOSIT:

Further deposits are identified
on 2 additional sheets:

X

Name of Depository: American Type Culture Collection
Address of Depository: 10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Accession Number	Date of Deposit	Accession Number	Date of Deposit
203027	26-Jun-1998	209568	6-Jan-1998
203069	27-Jul-1998	209580	14-Jan-1998
203070	27-Jul-1998	209603	29-Jan-1998
203071	27-Jul-1998	209626	12-Feb-1998
203081	30-Jul-1998	209627	12-Feb-1998
203105	13-Aug-1998	209628	12-Feb-1998
203181	9-Sep-1998	209641	25-Feb-1998
203331	8-Oct-1998	209645	25-Feb-1998
203364	19-Oct-1998	209646	25-Feb-1998
203484	17-Nov-1998	209647	25-Feb-1998
203499	1-Dec-1998	209651	4-Mar-1998
203517	10-Dec-1998	209683	20-Mar-1998
203570	11-Jan-1999	209745	7-Apr-1998
203648	9-Feb-1999	209746	7-Apr-1998
203858	18-Mar-1999	209782	20-Apr-1998
203979	29-Apr-1999	209852	7-May-1998
209007	28-Apr-1997	209853	7-May-1998
209008	28-Apr-1997	209877	18-May-1998
209009	28-Apr-1997	209878	18-May-1998
209010	28-Apr-1997	209889	22-May-1998
209011	28-Apr-1997	209965	11-Jun-1998
209012	28-Apr-1997	97897	26-Feb-1997
209022	8-May-1997	97898	26-Feb-1997
209043	15-May-1997	97899	26-Feb-1997
209044	15-May-1997	97900	26-Feb-1997
209045	15-May-1997	97903	26-Feb-1997
209046	15-May-1997	97921	7-Mar-1997
209049	15-May-1997	97922	7-Mar-1997
209070	22-May-1997	97923	7-Mar-1997
209071	22-May-1997	97924	7-Mar-1997
209072	22-May-1997	97955	13-Mar-1997
209073	22-May-1997	97957	13-Mar-1997

Applicant's File	International Application
Reference Number: PS904PCT	Number: Unassigned

Accession Number	Date of Deposit		Accession Number	Date of Deposit
209074	22-May-1997		97958	13-Mar-1997
209075	22-May-1997		97974	4-Apr-1997
209076	22-May-1997		97975	4-Apr-1997
209080	29-May-1997		97976	4-Apr-1997
209081	29-May-1997		97977	4-Apr-1997
209082	29-May-1997		97978	27-Mar-1997
209083	29-May-1997		97979	27-Mar-1997
209084	29-May-1997		PTA-1201	13-Jan-2000
209085	29-May-1997		PTA-1543	21-Mar-2000
209086	29-May-1997		PTA-1544	21-Mar-2000
209089	5-Jun-1997		PTA-161	1-Jun-1999
209090	5-Jun-1997		PTA-163	1-Jun-1999
209118	12-Jun-1997		PTA-2069	9-Jun-2000
209119	12-Jun-1997		PTA-2070	9-Jun-2000
209124	19-Jun-1997		PTA-2071	9-Jun-2000
209125	19-Jun-1997		PTA-2072	9-Jun-2000
209126	19-Jun-1997		PTA-2073	9-Jun-2000
209138	3-Jul-1997		PTA-2074	9-Jun-2000
209139	3-Jul-1997		PTA-2075	9-Jun-2000
209141	9-Jul-1997		PTA-2076	9-Jun-2000
209145	17-Jul-1997		PTA-2077	9-Jun-2000
209146	17-Jul-1997		PTA-2078	9-Jun-2000
209147	17-Jul-1997		PTA-2079	9-Jun-2000
209148	17-Jul-1997		PTA-2080	9-Jun-2000
209177	24-Jul-1997		PTA-2081	9-Jun-2000
209178	24-Jul-1997		PTA-2082	9-Jun-2000
209179	24-Jul-1997		PTA-2083	9-Jun-2000
209180	24-Jul-1997		PTA-2982	26-Jan-2001
209194	1-Aug-1997		PTA-322	9-Jul-1999
209195	1-Aug-1997		PTA-499	11-Aug-1999
209197	8-Aug-1997		PTA-536	13-Aug-1999
209215	21-Aug-1997		PTA-622	2-Sep-1999
209224	28-Aug-1997		PTA-623	2-Sep-1999
209225	28-Aug-1997		PTA-841	13-Oct-1999
209226	28-Aug-1997		PTA-842	13-Oct-1999
209235	4-Sep-1997		PTA-843	13-Oct-1999
209236	4-Sep-1997		PTA-844	13-Oct-1999
209241	12-Sep-1997		PTA-845	13-Oct-1999
209242	12-Sep-1997		PTA-846	13-Oct-1999
209243	12-Sep-1997		PTA-847	13-Oct-1999
209244	12-Sep-1997		PTA-848	13-Oct-1999
209277	18-Sep-1997		PTA-849	13-Oct-1999

Applicant's File	International Application
Reference Number: PS904PCT	Number: Unassigned

Accession Number	Date of Deposit	Accession Number	Date of Deposit
209299	25-Sep-1997	PTA-855	18-Oct-1999
209300	25-Sep-1997	PTA-867	26-Oct-1999
209324	2-Oct-1997	PTA-868	26-Oct-1999
209346	9-Oct-1997	PTA-869	26-Oct-1999
209368	16-Oct-1997	PTA-870	26-Oct-1999
209407	23-Oct-1997	PTA-871	26-Oct-1999
209423	30-Oct-1997	PTA-872	26-Oct-1999
209463	14-Nov-1997	PTA-883	28-Oct-1999
209511	3-Dec-1997	PTA-884	28-Oct-1999
209551	12-Dec-1997	PTA-885	28-Oct-1999
209563	18-Dec-1997		

EUROPE

In respect of those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which the application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28(4) EPC).

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by an applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

What Is Claimed Is:

1. Use of a polypeptide for the preparation of a diagnostic or pharmaceutical composition for diagnosing or treating cancer or other hyperproliferative disorder, wherein said polypeptide comprises an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(b) a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(c) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(d) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;

(e) a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;

(f) a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and

(g) a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

2. Use of the polypeptide of claim 1, wherein said wherein said polypeptide comprises a heterologous amino acid sequence.

3. Use of a polypeptide for the preparation of a diagnostic or pharmaceutical composition for diagnosing or treating cancer or other hyperproliferative disorder, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of:

(a) a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(b) a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(c) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(d) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;

(e) a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;

(f) a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and

(g) a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

4. Use of the polypeptide of claim 3, wherein said polypeptide comprises a heterologous amino acid sequence.

5. Use of an antibody or fragment thereof for the preparation of a diagnostic or pharmaceutical composition for diagnosing or treating cancer or other hyperproliferative disorder, wherein said antibody or fragment thereof binds a polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(b) a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(c) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(d) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;

(e) a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;

(f) a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and

(g) a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

6. Use of an antibody or fragment thereof for the preparation of a diagnostic or pharmaceutical composition for diagnosing or treating cancer or other hyperproliferative disorder,

wherein said antibody or fragment thereof binds a polypeptide selected from the group consisting of:

(a) a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(b) a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(c) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(d) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;

(e) a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;

(f) a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and

(g) a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

7. Use of a nucleic acid molecule for the preparation of a diagnostic or pharmaceutical composition for diagnosing or treating cancer or other hyperproliferative disorder, wherein said nucleic acid molecule comprises a polynucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polynucleotide fragment of SEQ ID NO:X as referenced in Table 1A;

(b) a polynucleotide encoding a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(c) a polynucleotide encoding a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(d) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(e) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;

(f) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;

(g) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and

(h) a polynucleotide encoding a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

8. Use of the nucleic acid molecule of claim 7, wherein said nucleic acid molecule comprises a heterologous polynucleotide sequence.

9. Use of a nucleic acid molecule for the preparation of a diagnostic or pharmaceutical composition for diagnosing or treating cancer or other hyperproliferative disorder, wherein said nucleic acid molecule comprises a polynucleotide sequence selected from the group consisting of:

(a) a polynucleotide fragment of SEQ ID NO:X as referenced in Table 1A;

(b) a polynucleotide encoding a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(c) a polynucleotide encoding a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(d) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(e) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;

(f) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;

(g) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and

(h) a polynucleotide encoding a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

10. Use of the nucleic acid molecule of claim 9, wherein said nucleic acid molecule comprises a heterologous polynucleotide sequence.

11. Use of an agonist or antagonist for the preparation of a pharmaceutical composition for treating cancer or other hyperproliferative disorder, wherein said agonist or antagonist binds a polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(b) a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(c) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(d) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;

(e) a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;

(f) a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and

(g) a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

12. Use of an agonist or antagonist for the preparation of a pharmaceutical composition for treating cancer or other hyperproliferative disorder, wherein said agonist or antagonist binds a polypeptide selected from the group consisting of:

(a) a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(b) a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(c) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

- (d) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;
- (e) a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;
- (f) a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and
- (g) a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

13. A polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

- (a) a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;
- (b) a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;
- (c) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;
- (d) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;
- (e) a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;
- (f) a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and
- (g) a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

14. The polypeptide of claim 13, wherein said polypeptide comprises a heterologous amino acid sequence.

15. Use of the polypeptide of claim 13 for identifying a binding partner comprising:

- (a) contacting the polypeptide of claim 13 with a binding partner; and
- (b) determining whether the binding partner increases or decreases activity of the polypeptide.

16. A polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(b) a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(c) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(d) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;

(e) a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;

(f) a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and

(g) a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

17. The polypeptide of claim 16, wherein said polypeptide comprises a heterologous polypeptide sequence.

18. Use of the polypeptide of claim 16 for identifying a binding partner comprising:

(a) contacting the polypeptide of claim 16 with a binding partner; and

(b) determining whether the binding partner increases or decreases activity of the polypeptide.

19. An antibody or fragment thereof that binds a polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(b) a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(c) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

- (d) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;
- (e) a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;
- (f) a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and
- (g) a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

20. An antibody or fragment thereof that binds a polypeptide selected from the group consisting of:

- (a) a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;
- (b) a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;
- (c) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;
- (d) a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;
- (e) a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;
- (f) a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and
- (g) a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

21. A nucleic acid molecule comprising a polynucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

- (a) a polynucleotide fragment of SEQ ID NO:X as referenced in Table 1A;
- (b) a polynucleotide encoding a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;
- (c) a polynucleotide encoding a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(d) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(e) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;

(f) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;

(g) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and

(h) a polynucleotide encoding a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

22. The nucleic acid molecule of claim 21, wherein said nucleic acid molecule comprises a heterologous polynucleotide sequence.

23. A recombinant vector comprising the nucleic acid molecule of claim 21.

24. A recombinant vector comprising the nucleic acid molecule of claim 22.

25. A recombinant host cell comprising the recombinant vector of claim 23.

26. A recombinant host cell comprising the recombinant vector of claim 24.

27. A nucleic acid molecule comprising a polynucleotide sequence selected from the group consisting of:

(a) a polynucleotide fragment of SEQ ID NO:X as referenced in Table 1A;

(b) a polynucleotide encoding a full length polypeptide of SEQ ID NO:Y or a full length polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(c) a polynucleotide encoding a predicted secreted form of SEQ ID NO:Y or a secreted form of the polypeptide encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(d) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A;

(e) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA Clone ID in ATCC Deposit No:Z corresponding to SEQ ID NO:Y as referenced in Table 1A, wherein said fragment has biological activity;

(f) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y as referenced in Table 1B;

(g) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y as referenced in Table 2; and

(h) a polynucleotide encoding a predicted epitope of SEQ ID NO:Y as referenced in Table 1B.

28. The nucleic acid molecule of claim 27, wherein said nucleic acid molecule comprises a heterologous polynucleotide sequence.

29. A recombinant vector comprising the nucleic acid molecule of claim 27.

30. A recombinant vector comprising the nucleic acid molecule of claim 28.

31. A recombinant host cell comprising the recombinant vector of claim 29.

32. A recombinant host cell comprising the recombinant vector of claim 30.

Sequence List

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<210> 17

<211> 1722

<212> DNA

<213> Homo sapiens

<400> 17

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<210> 18

<211> 1453

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (946)..(946)

<223> n equals a,t,g, or c

<400> 18

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<210> 19

<211> 1752

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (356)..(356)

<223> n equals a,t,g, or c

<400> 19

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<210> 20

<211> 2321

<212> DNA

<213> Homo sapiens

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<221> misc_feature

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<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (880)..(880)

<223> n equals a,t,g, or c

<400> 20

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2321

<210> 21
 <211> 843
 <212> DNA
 <213> Homo sapiens

<400> 21
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 <211> 1382
 <212> DNA
 <213> Homo sapiens

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 <213> Homo sapiens

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 <223> n equals a,t,g, or c

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 <211> 1357
 <212> DNA
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<210> 25

<211> 1313

<212> DNA

<213> Homo sapiens

<400> 25

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tccagtcatt	ggggttgacc	ccaggaaaag	gtatggtttg	gggtaagagg	actcttcagt	600
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<210> 26

<211> 1003

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (990)..(990)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (1002)..(1002)

<223> n equals a,t,g, or c

<400> 26

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<210> 27

<211> 1963

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (335)..(335)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (1959)..(1959)

<223> n equals a,t,g, or c

<400> 27

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cagttgcaga atgaagaaga gtctggagaa cctgaacagg ctgcagggtga tgctcctcca 300
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catactgtac tacttgcttt tacaatgtgt tagcagaaac cagtgggtta taatgtagaa 1800
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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaa 1963

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<210> 28
<211> 796
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<222> (748)..(748)
<223> n equals a,t,g, or c

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<400> 28
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ttcttagcct cccacctcct tgctgtggag cagcttcatg taccatgatg catattcaga 180
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cgggtgttct cctaattcta tcccwccct acccccctgc ccccaaaaag gccccagtg 480
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<210> 29
<211> 1256
<212> DNA
<213> Homo sapiens

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<400> 29
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<210> 30
<211> 752

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<212> DNA

<213> Homo sapiens

<400> 30

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gtaagtaaca	tttttttga	taggtatacc	atgatttgtt	gatgaacaaa	tttacctgtt	660
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<210> 31

<211> 2243

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (929)..(929)

<223> n equals a,t,g, or c

<400> 31

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<210> 32

<211> 1624

<212> DNA

<213> Homo sapiens

<400> 32

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<210> 33

<211> 879

<212> DNA

<213> Homo sapiens

<400> 33

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<210> 34
<211> 2761
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1006)..(1006)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (1376)..(1376)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (2211)..(2211)
<223> n equals a,t,g, or c

<400> 34
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gaatatgaga atatcatcca agattttaaat accaattacc aaaattttaca gctatcaaat 180
ggaagactca gggtttatgct atgccacgtt ttctcttctt tcctttttgt gatgggtgttc 240
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gcttctttac gtttggtctc tgcatkgtta tgacttaaag gctgcgctca aaataatctc 540
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gttatccaaa gaatgacaat ggtttgtttg ccaagtcttt ttgttttgtt gtgttttgtt 2160
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caaaaagaaa aaaaaaaatc aacacctaaa aatttacttt cttctagtca atttatttcg 2280
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c 2761

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<210> 35
<211> 755
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<222> (1)..(1)
<223> n equals a,t,g, or c

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<220>
<221> misc_feature
<222> (733)..(734)
<223> n equals a,t,g, or c

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<400> 35
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gacttggcct tgcgcttgcg ggcctcagcc gtgccgctcc acacgaagca ctggtagatg 660
gcccgaggt tctgcttcca gttgtccacc ttgaagctgc ccagggtgcga gcagcccgcc 720
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```

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<210> 36
<211> 2089
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (774)..(774)
<223> n equals a,t,g, or c

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<400> 36
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tcttctccc catcaggggc agtgcccacg tctttggagc tgcagcgagg gacggatggc 180
ggaacctctc agtccccttc agaggcgact gcaactcgcc cggccgtgcc tggactccct 240
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ccagtcttac cgatctgtgt ctgtgacttg actcctggag cctgcgatat aaattgctgc 360
tgcgacaggg actgctatct tctccatccg aggacagttt tctccttctg ccttccaggc 420
agcgtaaggt cttcaagctg ggtttgtgta gacaactctg ttatcttcag gagtaattcc 480
ccgtttcctt caagagtttt catggattct aatggaatca ggcagttttg tgtccatgtg 540

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aacaactcaa	acttaaacta	tttccagaag	cttcaaaagg	tcaatgcaac	caacttccag	600
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agcttgctga	gacaacctgc	aggagttgga	gctgggggac	tctgtgctga	aagnaatcct	780
gcaggtttcc	tagagagtaa	aagtacaact	tgcaactggt	ttttcaagaa	cctggctagt	840
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<210> 37

<211> 785

<212> DNA

<213> Homo sapiens

<400> 37

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aaatcagatt	gccaggaaga	aataggacgt	gacggtactg	ggccctgtga	ttctcccagc	180
ccttgcaagt	cgctaggtga	gaggaaaagc	tctttacttc	cgccctggc	agggtactct	240
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acatcacaa	gtcattttga	taggagcggt	ttgttatttt	tacaaggcag	aatgggggtg	720
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gccgc						785

<210> 38

<211> 1458

<212> DNA

<213> Homo sapiens

<400> 38

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aaaaaaaaaa aaaaaaaaaa 1458

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<210> 39

<211> 2657

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (179)..(179)

<223> n equals a,t,g, or c

<400> 39

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<210> 40

<211> 1503

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (6)..(6)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (18)..(18)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (41)..(41)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (1501)..(1501)

<223> n equals a,t,g, or c

<400> 40

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aatctgccct acaaaattht tttggcttaa acgtcaaaag ccgtgacaat ttgttctttg 1380
atgtgattgt atttccaatt tcttggtcat gtaagatttc aataaaacta aaaaatctat 1440
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naa 1503

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<210> 41
<211> 1280
<212> DNA
<213> Homo sapiens

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<400> 41
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ttatcactgc tgcgtgctg gctgctgctg tcagctagct ttgtgacttt cagcaccctc 180
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tccacatctg acgttcttag ctctttagag tcccaaaac tatctgttac catatttcat 480
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cacatcagat gctttacttt ggcaaatcat agaactttct gtcaataggg ataataatgg 600
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aaccacaagt catcattgac 1280

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<210> 42
<211> 742
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<222> (707)..(707)
<223> n equals a,t,g, or c

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<220>
<221> misc_feature
<222> (724)..(724)
<223> n equals a,t,g, or c

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<220>
<221> misc_feature
<222> (726)..(726)
<223> n equals a,t,g, or c

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<400> 42
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ttggagggca cttctttcgt ggtagtctt ttatttttat taatctctgt atccttagat 180
agtcctccaa caaccaaagg ttgggactct gtcttacata tctgggtgcc cctcatagt 240

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cagtaataag taagttgatt atatacagagc tatgtaactt atatttttta atgggttggat 300
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ttaactatit taaagtgaga agttcagtg cacttagtat tggttaacaat gttgcataac 420
caccaccttt atttaaagtt ccaaaaaaaa tgttctcctc taaaaggaaa ccccatccca 480
ttaagcagat actctccatt ccttccttcc tccagccccc agcaaccacc aatctgcttt 540
ctgtctctat ggatttatct attcttgcta ttttatataa atcgaattgt atgagacctt 600
ttgtgtctgg cttctttcac ttagtacaag tttttgagat ttatttacat agtagcatgt 660
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aaananaaaa atgaccctcg ag 742

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<210> 43

<211> 1472

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)..(1)

<223> n equals a,t,g, or c

<400> 43

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ctgcattttg agcaaaaggt ggcttcccag ctctaacaag gtaactgggt agcatgacat 1440
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<210> 44

<211> 635

<212> DNA

<213> Homo sapiens

<400> 44

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taatcaggga aatgacaagt tacatactga tatccttgtt ttgctgatt ggagttgggt 180
gcattgaaaa agatcagtcg tgcccagtg tttgggggaa gaagcgtctt cacctgttgt 240
ttgtgggagg acagttgagg caggtgagga tgctgagagg tgagctcagc tgtgcctgtt 300
accgtccaca tgtgcaagcc cttcagctcg gtggtgttac ttgttttga gatgcagttt 360
cactcttgtc acccaggctg gagtgcatgg catgatctt gctcgctgca acatccgcct 420
ccccgggttca agcgattctc ctgtctctac taaaaataca aaaattagct ggggtgtgtg 480

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gtgctgcct ttaatcccag ctactcagaa ggctgaggtg caagaattgc ttgaacctgg 540
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 tagactgtct caaaaaaaaa aaaatgaccc tcgag 635

<210> 45
 <211> 1153
 <212> DNA
 <213> Homo sapiens

<400> 45
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 acactgggccc tggatctttc ttggtccatc agcctagcct tcaagtgggtg tgagcggcct 480
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 aaatgaccct cga 1153

<210> 46
 <211> 729
 <212> DNA
 <213> Homo sapiens

<400> 46
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 cccctcctgc tcagtctctt tgtactggg ctatttcttt gggttctgaa gagagagaga 180
 caagaagagt acattgaaga gaagaagaga gtggacattt gtcgggaaac tcctaacata 240
 tgccccatt ctggagagaa cacagagtag gacacaatcc ctacactaa tagaacaatc 300
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 aatccccact cactgctcac gatgccagac acaccaaggc tatttcctta tgagaatgtt 420
 atctagacag cagtgcactc ccctaagtct ctgctcaaaa aaaaaacaat tctcggccca 480
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 gttgactttt ttccaggata aattatctct gatgcttctt tagatttaag agttcataat 600
 tccatccact gctgagaat ctctcaaac ccagaagggt taatcacttc atcccaaaaa 660
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 aaaaaaaaa 729

<210> 47
 <211> 1079
 <212> DNA
 <213> Homo sapiens

<400> 47
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 ggctgagagg aggacacgga gggctctgct gaggttcctt cctgggttcc accaacaggg 180
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gtaagcatga	tactagtggg	tttaccagtg	tttcttccaa	ggagacatat	attttttaat	1020
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<210> 48

<211> 1959

<212> DNA

<213> Homo sapiens

<400> 48

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gatgacacag	aacgcttgcc	cagcaaatgc	gaagtgtgta	agctgctgag	cacagagcta	240
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gatacaggca	agaggaagag	acacgtgcct	tacagcgttt	cagagacaag	gctggaagag	360
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tcactgagat	atgccaaggg	tcagagtcag	accatggcaa	cactgaaagg	cctagtgcag	480
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ccgacgcgtc	ttgggtatcc	acaaaccag	tataatgagc	agcagagaaa	aacgcatgat	1920
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<210> 49

<211> 812

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature
 <222> (17)..(17)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (108)..(108)
 <223> n equals a,t,g, or c

<400> 49
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 cgtctcaaaa aaaaaaaaaa aaaaaactcg ag 812

<210> 50
 <211> 1756
 <212> DNA
 <213> Homo sapiens

<400> 50
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<210> 51
 <211> 2098
 <212> DNA
 <213> Homo sapiens

<400> 51
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 <212> DNA
 <213> Homo sapiens

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<211> 1280

<212> DNA

<213> Homo sapiens

<400> 53

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<210> 54

<211> 953

<212> DNA

<213> Homo sapiens

<400> 54

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<210> 55

<211> 1027

<212> DNA

<213> Homo sapiens

<400> 55

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<211> 1368

<212> DNA

<213> Homo sapiens

<400> 56

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1368

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 <212> DNA
 <213> Homo sapiens

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 <213> Homo sapiens

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<210> 59
 <211> 786
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 <213> Homo sapiens

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 <213> Homo sapiens

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<210> 61

<211> 537

<212> DNA

<213> Homo sapiens

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agccaaagccc	atcttcagct	gcctcaacac	cgccctgtct	gaggctgaga	agggccagtg	240
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ttcgggagag	gaggaggagg	gcaaagagaa	aaagactttc	cccatctctg	gggccagggg	360
tggagccaga	ggcaccgggt	acagatacgt	gtcccaagca	cagcccaggg	gaaagccacg	420
ccaggacacg	gccaagagtc	cccaccgcac	caagttcacc	ctgtccctcg	acgtccccac	480
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<210> 62

<211> 843

<212> DNA

<213> Homo sapiens

<400> 62

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tatgtgccca	gctggctgtg	gctggtaaag	gagctcgagg	ctttgggagg	ggagccctga	180
tccgcctgaa	tatctggccg	gcggtccaag	gggcctgcaa	acagctggag	gtctgtgagc	240
actgcgtgga	gggagacaga	gcgcgcaatc	tctccagctg	catgtgggag	cagtgcgggc	300
cagaggagcc	aggacactgt	gtggcccaat	ctgaggtggg	caaggaaggt	tgctccatct	360
acaaccgctc	agaggcatgt	ccagctgttc	accaccaccc	cacctatgaa	ccgaagacag	420
tcacaacagg	gagcccccca	gtccctgagg	cccacagccc	tggatttgac	ggggccagct	480
ttatcggagg	tgctgtgtcg	gtgttgagcc	tacaggcggt	ggctttcttt	gtgctgcact	540
tcctcaaggc	caaggacagc	acctaccaga	cgctaactcg	acccctttgg	gcctggactc	600
catcctgagg	ggaaaaggag	atgcagaggg	tggcctctgg	gcacccttgt	gggtaagcgg	660
ggggcggggg	cgggaaaaac	tctggccgcc	agtttttggc	tcctgcgggc	accaagcagg	720
ccaagtgttt	aatgcctgac	atctcctcct	gtcctggggc	tggaaacctgc	agctgagaaa	780
atccctcaac	cacctcgtct	cctccatcgc	ccctgctggg	ccccccagcc	tgacagtggg	840
ttg						843

<210> 63

<211> 849

<212> DNA

<213> Homo sapiens


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<400> 63
gaattcggca cgaggtataa tgccattctc ttctctgtg aagtgcctgt tcggggtgtt      60
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taagaggact ttaggttact gagtaccca tggatcatgt ttgcagagaa gtgtcacaga      180
gtgaaaactg tcttttcctt gatactacct ttagattcat atttgggaag accttcacta      240
atcatgacta cataagtatt cacttttact ttcttaaggc ctttttggtt tcattctttt      300
atagtaatgt ctaagccatc tggaattagt ttgttgatta tgcaagaaag ggatcgaagt      360
gctttttctg agtcattatc cacatgccga aacattttatt gaatagccct ttccttattg      420
atctgaaaac accttcttat aaaaccttgc attgggtttt ggacttgctg tgctttcagg      480
agtcagaaga acattctttt gattatkgta gctttacatw aataatacat ttkggccggg      540
tgcggtggct cactgatgta atcctagcat ttggggagac tgaggcaggc ggaacacctg      600
aggtcagggg ttcaagacca gactggccaa catggcaaaa ccccgctctc aaaaaaaaaa      660
aaaaaaaaaa aattagctgg gcatggtggt gcctgcctga aatcccagct actttggggag      720
gctgaggcag gagaacctct tgagcctggg aggtagaggc tgcagtgagc cgagcttgca      780
ccactgcact ccaacttggg taacagagtg agactccatc tcaaaaaaaaa aaaaaaaaaa      840
aaaactcga

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<210> 64
<211> 2434
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<222> (10)..(10)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc_feature
<222> (12)..(12)
<223> n equals a,t,g, or c

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<220>
<221> misc_feature
<222> (27)..(27)
<223> n equals a,t,g, or c

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<220>
<221> misc_feature
<222> (73)..(73)
<223> n equals a,t,g, or c

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<220>
<221> misc_feature
<222> (75)..(75)
<223> n equals a,t,g, or c

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<220>
<221> misc_feature
<222> (103)..(103)
<223> n equals a,t,g, or c

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<220>
<221> misc_feature
<222> (130)..(130)
<223> n equals a,t,g, or c

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<400> 64
ctgggggtan tncaagaacc ctctgtngga cttagatgtc aagctctttc ctttgggcag      60
cgtgtttcct ttntncgagt agtgtgctgt gtaactaaa ttngccggtt cgctttccat      120

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ttcctgacan	ttgagatgga	atgccttgac	cattgggtgct	ctgacagaga	agtcattggag	180
tcattggccat	ttcctgggtg	cccttttgga	atgtgatcct	gtagtagag	gttttctagc	240
ttctactaag	atatttcttt	ccctaaccat	catacacttg	gcatgtttca	ttcccatctc	300
ctttccctc	accttaaagg	agactacccc	tttgcccat	attgtcaacc	taattttctc	360
tcgtactctc	tctagtgaat	gatgtgctac	caagtatatg	ccaggctgtg	agaggattat	420
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gctagtgtct	gctgagtgc	tactaagaaa	gcaattccaa	atagatgtat	acatctagag	1020
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tatcatgtgc	ctttgaaatt	tgacagctga	tttgggtgtt	ggatttctgc	ccagccattt	1320
atcagtatta	tcattttatt	cagtagctgg	caggtgtatt	agacaaacga	gacttaggta	1380
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gaatcaaa	tagcacagaa	atgaactaag	tatatcccat	ttggaattat	attttgatac	1980
tatttaaaat	ggtttcacct	gttaaagggc	caacagaact	cttggtttta	cttttgtaat	2040
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gtagggatat	gatactttac	aggaattata	tatgaaaaaa	gtttttgaaa	tgtatttttg	2160
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aaaaatgttt	tatatttttt	tttaagtaaa	atggaccag	taagaaaatt	aaaaatacca	2340
gaacataaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	2400
aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaa			2434

<210> 65

<211> 872

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (844)..(844)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (858)..(858)

<223> n equals a,t,g, or c

<400> 65

ggggaagttc	ttcactgcct	tgcatttgac	tccagatccc	tccatcctcc	cagagccttg	60
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ttgctgcttc	acttgctcac	ttaatctccc	ttttcatagg	gctgtgtgtt	ttacttctgg	180
gaagtctgt	ttaccctgga	acagaaactc	tcttccctaa	aagttgattt	tattgaccca	240
tggaggccag	agacacttag	gcatattttc	cctccagact	agaagcttct	gaggaggacc	300

tcctgagtct	gcaccctggc	tccctgctgt	gctgagggcc	cccgtgttaa	cctcacgttg	360
tgctcctct	gattcagagg	gcccagtggt	gttctgtcag	ccaggcagtg	gccccagctc	420
tacagaaatg	agttgtcatt	gcacccctagg	gccagggtct	tcgtgcttgt	gtgtgttacg	480
tggaaagtatg	tggacaccaa	gtgttccttg	atggccacag	cctgcgaagg	aaactggggc	540
cagcagctgc	tctgtgtttt	cagccaacaa	tggctcctgc	ccactgccgc	tgcataacca	600
ccagaggcag	gcttctcttg	acacaggcct	gtcgttgagg	catgtgcctg	gcgagtccta	660
tttctattcc	cctgtgggtt	agggacaggc	agctgtacct	tcagtgtgtt	gctggggcag	720
gagaatcgct	tgaaccggga	ggcggagggt	gcagtgagcc	aaaattgcac	cactgcactg	780
cagtctgcag	gacagagaga	ggctmtatct	caaaaaaaaa	aaaaaaaaaa	actcgagggg	840
gggnccggga	cccaattngc	catataggaa	aa			872

<210> 66

<211> 1932

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (2)..(2)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (1022)..(1022)

<223> n equals a,t,g, or c

<400> 66

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gggaaatagg	ccccggggg	cggtggcgcc	ggcggggcca	tggcgcgag	acccccggcg	120
ccggccgcct	ccggggagga	gttctccttc	gtcagcccgc	tggtgaaata	cctgctcttc	180
ttcttcaaca	tgctctcttg	gggtatttcc	atggtgatgg	tggctgtggg	tgtctacgct	240
cggtctaatga	agcatgcaga	agcagcccta	gcctgcctgg	cagtggaccc	tgccatcctg	300
ctgatcggtg	tgggtgtcct	catgttctct	ctcaccttct	gtggctgcat	tgggtccctc	360
cgcgagaaca	tctgcctcct	gcagacgttc	tccctctgcc	tcaccgctgt	gttccctgctg	420
cagctggccg	ctgggatcct	gggcttcgtc	ttctcagaca	aggctcgagg	gaaagtgagt	480
gagatcatca	acaatgccat	tgtgcactac	cgagatgact	tggatctgca	gaacctcatt	540
gattttggcc	agaaaaagtt	tagctgctgt	ggagggattt	cctacaagga	ctgggtctcag	600
aacatgtatt	tcaactgctc	agaagacaac	ccagctcgag	agcgtgctc	tgtgccttac	660
tcctgttgct	tgctactcct	tgaccaggca	gtgatcaaca	ctatgtgtgg	ccaaggatg	720
caggcctttg	actacttgga	agctagcaaa	gtcatctaca	ccaatggctg	tattgacaag	780
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atcaagctac	agctctacaa	ccagcagcac	cgggctgacc	catgggtactg	agaatccatc	960
ctgcacctcc	tcaccatgga	aactggcaag	cctcataaac	gaacagcagt	gggtgctgaa	1020
ancagcacca	aatggagatt	tggattccag	ccccccagtg	acagcccagt	gggaagaagc	1080
aaactccaga	tgggcagaag	gcagggtgca	cagggtggctc	cagtctcagg	aggatgcgcc	1140
tcctctcccc	catcccagcc	ctcagcattg	tgccagagtg	atacccttaa	gtgtttgggt	1200
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tgctttttca	ccgaggcact	gccaccacca	gctctascag	ggatgctcct	gagcttggcg	1320
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ccaccccat	cccctgcac	ggagctcagt	attcctacag	ggtaagaggt	aggaatcttg	1860
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aaggcggcc	gc					1932

<210> 67
 <211> 1853
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1840)..(1840)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (1851)..(1851)
 <223> n equals a,t,g, or c

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<400> 67
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ctgtgtatatt ctcattggcct gcctgggagc ccccatctcc agcctgctgt gctggctact      120
tctggcactt atagcccttg agatagtacc gccagcagct ccctgtgaag tgctaaccacc      180
ccttcaaagc agcaccaacc caattgtgaa caagctagga gtaaaagacg taaatgaatt      240
ggtcacccca atgcagggga tacagacttg ttttaataata aaaaagaagt ggccttaacc      300
gtgcagggct tgcaggcctt tgtaggcatg ggagcatgct gtgatccctg gttctgtgct      360
aaacactcaa aagggtcttc tgactcaagt ggaggtgata aaccttttca atagtaacag      420
gagagagtgt gatatacaag tgccmgaasy cctcacggac caacatttag cacagacatt      480
caaactgctg aaagawccaa wcagaactca actgaaaaaa acagaccttt taagaaaagc      540
aatagatctt aatttggtgg caagatccct ggtttacctt ttgaagtcaa aatgttcaat      600
acatcacccg agcttgactt ttgagcactt ggcaagattg ttttttgcca cttgacacaa      660
gtatgatgtc cagctatgca aaatgactgt ttgatctgcc ttttcagtgt atttgtgtgg      720
cgatgtctgt aaaatgccag aagcctctta tgttattgct gctgctgcta ccagccagca      780
actgcagagg ccatgctgag gtgcctcctt gccaccagcc gttgggaaat gcctaccatg      840
ctgccccgga tgcacaagct caaaacgctg cagaagttac acaactgctc ccataatctg      900
gactctccaa aaccgtgatg ccacgaagga aggtcaagtt ttaaaatggt aaagactgct      960
tgccctctgt cctgagacta aacagtatac atactaacta cattgacaaa gaaatcctat      1020
ctgataatgt agcccgtgta cgaattttga agcctcgggt accctaacca atatgtagct      1080
tttaatttgc atcaaaactt ttacaaagat gttttgctat tgtttctata tacttcaaga      1140
atgttcattt ttacaaataa gttgaacaag acagcctaag ttagatgcac cgaagtacta      1200
gaaatatcgc tagcctctgt tctccagttt agctttcaaa accaaatgag ccattgtataa      1260
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cctttgaaag tttccagttg tgtgggctgc tgtctcacct cccaccaatt tctccttct      1380
ccttatgggt ctaaaacctc aaagctgagg agggctgcag gacccttagc agattcagtg      1440
tgtcacctt gtccctgtgt cagcccaagg ctctcctaaat gaaagacatc ggttacctgc      1500
ttatgggaag actcttcatt ctgatcggtt cttgcattga aataaccatg tggaagaaca      1560
atgaatcgat taatgatgac atgtacaacc atatttaaag agcaatagtg tccgtgtgtc      1620
atgaaaaact tatttgtaaa cgtttatatg gtatgatttt gattttatgt atgttcataa      1680
atcctgcact gtatgatata tgtgagttaa aacattgggt catgaattta ttttcaaagt      1740
ataaaacaca tcacttaaac attttatgtg tcaaataaaa tttgattatg taaaaaaaaa      1800
aaaaaaaaac tcgagggggg gcccggrccc aattcgccan atggagatcc naa      1853

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<210> 68
 <211> 1061
 <212> DNA
 <213> Homo sapiens

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<400> 68
ggcacgagga ttctaggaca gggatggggg tgcagcactg atccaggacc cagaatggag      60
gcatcatgga ggggtccccg ggatggctgg tgctctgtgt gctggccata tcgctggcct      120
ctatggtgac cgaggacttg tgccgagcac cagacgggaa gaaaggggag gcaggaagac      180
ctggcagacg gggggcgcca ggccctcaagg gggagcaagg ggagccgggg gccctggca      240
tccggacagg catccaaggc cttaaaggag accaggggga acctggggcc tctggaaacc      300
cgggcaaggt gggctaccca gggcccagcg gcccctcgg agcccggtgc atccgggaa      360
ttaaaggcac caagggcagc ccaggaaaca tcaaggacca gccgaggcca gccttctccg      420

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ccattcggcg	gaacccccca	atggggggca	acgtgggtcat	cttcgacacg	gtcatcacca	480
accaggaaga	accgtaccag	aaccactccg	gccgattcgt	ctgcactgta	cccggctact	540
actacttcac	cttcagggtg	ctgtcccagt	gggaaatctg	cctgtccatc	gtctcctcct	600
caagggggcca	ggtccgacgc	tccctgggct	tctgtgacac	caccaacaag	gggctcttcc	660
aggtgggtgc	agggggcatg	gtgcttcagc	tgagcagggg	tgaccaggtc	tgggttgaaa	720
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aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	a		1061

<210> 69

<211> 920

<212> DNA

<213> Homo sapiens

<400> 69

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aaacagtgtc	gcctgcctcc	tgtggggaat	gcaggatggg	gcaatgccct	ggcagcaggg	180
tcttgccctc	gctgatgcaa	ctgtggctgc	tctgtgtg	acagatcatg	tgcttggag	240
ccttcctgca	gcagggcagt	gtcagaaagt	ggaagagtgg	tgtgagcagc	ttccccggg	300
aaagcctggc	tgagcaactg	accttgagca	agcactgcag	atggcccttg	ttcctgccc	360
gctcctccag	ctgggagctc	tcagcccctg	gtaaattctg	gcagtgaag	acacattagc	420
acctccccct	acaatgaggc	acctatctag	acaacttggc	tgtccgggct	taacctgcgt	480
ggcaggggaag	gacgcctgcc	cagccttagc	ctctacgcaa	tggtggaggc	agggagggag	540
agaaccacac	agctccccctc	atttcccagc	agcccccatg	gagcctagtc	aacaggggtg	600
ggtcacaggc	taaatgagca	aagatgtgag	ctaataact	ggtagggtgc	atgggggctt	660
tcagagctgg	gtaaggaggg	aaagagatgg	agatactgg	tccccactcc	ttaacgtgcc	720
acctgccttc	cctgtccttt	acctccctc	attctgtctg	acctgaggaa	aatgcaaggg	780
aggctaggcc	tagtggctca	tgctgtcat	cccaacactt	tgggagactg	aggtgggaga	840
atcacttgag	cctaggagtt	tgagaccagc	ctagggaaca	tagtgagact	ttcgtctcta	900
caaaaaaaaa	aaaaaaaaaa					920

<210> 70

<211> 601

<212> DNA

<213> Homo sapiens

<400> 70

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<210> 71

<211> 1356

<212> DNA

<213> Homo sapiens

<400> 71

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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa 1356

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<210> 72

<211> 1411

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1395)..(1395)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (1397)..(1397)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (1401)..(1401)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (1408)..(1408)

<223> n equals a,t,g, or c

<400> 72

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tacgcgtgca acganancag ngtcgagngg t 1411

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<210> 73

<211> 2229

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (2227)..(2227)

<223> n equals a,t,g, or c

<400> 73

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aaaaaaaaa 2229

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<210> 74
 <211> 1554
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (695)..(695)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (874)..(874)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (1190)..(1190)
 <223> n equals a,t,g, or c

<400> 74
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<210> 75
 <211> 2083
 <212> DNA
 <213> Homo sapiens

<400> 75
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<210> 76

<211> 427

<212> DNA

<213> Homo sapiens

<400> 76

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<210> 77

<211> 863

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (7)..(7)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (298)..(298)

<223> n equals a,t,g, or c

<400> 77

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<210> 78

<211> 1276

<212> DNA

<213> Homo sapiens

<400> 78

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<210> 79

<211> 2494

<212> DNA

<213> Homo sapiens

<400> 79

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<210> 80

<211> 1630

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (527)..(527)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (546)..(546)

<223> n equals a,t,g, or c

<400> 80

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<210> 81

<211> 1860

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (912)..(912)

<223> n equals a,t,g, or c

<400> 81

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<210> 82

<211> 1509

<212> DNA

<213> Homo sapiens

<400> 82

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<210> 83

<211> 967

<212> DNA

<213> Homo sapiens

<400> 83

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<210> 84

<211> 885

<212> DNA

<213> Homo sapiens

<220>
 <221> misc_feature
 <222> (233)..(233)
 <223> n equals a,t,g, or c

<400> 84
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<210> 85
 <211> 853
 <212> DNA
 <213> Homo sapiens

<400> 85
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<210> 86
 <211> 400
 <212> DNA
 <213> Homo sapiens

<400> 86
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<210> 87
 <211> 1261
 <212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (481)..(481)

<223> n equals a,t,g, or c

<400> 87

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<210> 88

<211> 639

<212> DNA

<213> Homo sapiens

<400> 88

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<210> 89

<211> 3576

<212> DNA

<213> Homo sapiens

<400> 89

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<210> 90

<211> 1262

<212> DNA

<213> Homo sapiens

<400> 90

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gaacttgctg	gagtaataga	gggaaaacct	ctgcctgatt	ctaaatcaga	tctttgtcct	360
atactcggac	aattatgggt	tcataattta	ttatttttta	ttttctgggt	ttaacaaatg	420
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caaatagttc	aagatagcca	agatgaccaa	ttctgccagg	tggcaagcct	gatcttgcaa	1200
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<210> 91

<211> 614

<212> DNA

<213> Homo sapiens

<400> 91

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gctgcccctt	cagtgatgcc	aaccttgga	gatgccctca	tcctgtacct	gcatctggtc	180
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gcagctggca	gtagccctcc	tctctggctg	ccccattggc	cacatctctg	gcctgctaga	540
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aaaaaaaaaa	aaaa					614

<210> 92

<211> 958

<212> DNA

<213> Homo sapiens

<400> 92

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ccgggtccagg tyggaatgaa acattttacaa aaattgacat ttccttatgc atagatatatt 900
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<210> 93
<211> 712
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (20)..(20)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (44)..(44)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (56)..(56)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (128)..(128)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (625)..(625)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (692)..(692)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (699)..(699)
<223> n equals a,t,g, or c

<400> 93
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caccgcgntg gcggccgctc tagaactagt ggatcccccg ggctgcagga ttcggcacga 180
ggtttcctgt cagtgtctatt gagattttat tttattaatg tctgcactta gttttacttc 240
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taggttacca gatttgatag aagcacataa gactacttac tgcttttagtc tcaattatta 420
attgagaaat tatcaattaa caataaggat ttctcttatt tttccccaag ataagttata 480
tatttaaagt gtgttttata gtagaaagg tttagaatat ttgggttgct acattaattg 540
aaatggcagc tgaagatgtg atttccagcc agggatttat taaaaaaaaa aaaaaaaaaac 600
tcgagggggg gccgtacca atcgnctat agtgagtcgt atacaatcac gggcgctcgtt 660
acacgtcggg ctggaaacct gcgtaccact ancgtgcnc acacccttc gc 712

<210> 94
<211> 1106
<212> DNA
<213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1017)..(1017)
 <223> n equals a,t,g, or c

<400> 94
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 ttatggtcct ggacagaagg taagcttcct tgcaacttcc ctgggtccgg gggtagagtt 240
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 gaccaaaggc caagttctgt gtcccatgg gagattaaaa cccaagcccc tatgtctagg 360
 tccagtgtcc actgatttct ctaattgtga gtctttctgc ttacctagta cctagagttt 420
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 ccgacttgaa actcacagtc gtcccctcag aaaggcaggg caaatgttgt tatttccaat 720
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 gaccggagcc ccagatgcgc tgggtgctact gatgtcccgt gccgggcatg agcccttctg 840
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 ttaaaaaaaa aaaaaaaaaa ctcgag 1106

<210> 95
 <211> 1089
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (353)..(353)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (528)..(528)
 <223> n equals a,t,g, or c

<400> 95
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 agctgtggaa atttatacct cccgggtgct ggaggctgtt aatgggacag atgctcgggt 240
 aaaatgcact ttctccagct ttgcccctgt ggggtgatgct ctaacagtga cctggaattt 300
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 aagagctcat aaagtgggtg agataaaatc aaaagaagag gaaaggctca accaagagaa 720
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aaaaaaaa

1089

<210> 96
 <211> 1254
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1036)..(1036)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (1069)..(1069)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (1100)..(1100)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (1165)..(1165)
 <223> n equals a,t,g, or c

<400> 96
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 tttctcctac cagtaccctg cccacacccc ctacagcccc cagcctccac cctaccatga 180
 gctttcatct tacacctatg gtgggggcag tgccagcagc cagcatagtg agggcagccg 240
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 ggcccccgag tccaagtccg gcagtggcag tgagtctgag ccctccagcc gagggggcag 360
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 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa 1254

<210> 97
 <211> 865
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (365)..(365)
 <223> n equals a,t,g, or c

<400> 97

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<210> 98

<211> 1139

<212> DNA

<213> Homo sapiens

<400> 98

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atccccccaa	tattgggtgc	cctggagggt	ccaatcctgc	ccaccacca	cctattaatc	180
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<210> 99

<211> 1222

<212> DNA

<213> Homo sapiens

<220>

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<222> (772)..(772)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (796)..(796)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (823)..(823)

<223> n equals a,t,g, or c

<220>
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 <222> (855)..(855)
 <223> n equals a,t,g, or c

<400> 99
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 aaaaaaaa aaaaaaactc ga 1222

<210> 100
 <211> 367
 <212> DNA
 <213> Homo sapiens

<400> 100
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 gaattactta cagaaaccaa cctttgcatt aggtgagctt taccctcctc tgataaatct 240
 ctgggaagca ggaaaagaaa aaagtacatc actgaaagta aaagcaactg ttataggttt 300
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 aaaaaa 367

<210> 101
 <211> 875
 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (66)..(66)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (872)..(872)
 <223> n equals a,t,g, or c

<400> 101
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ggtgcagctc agcaccccc cttatgcaga ctgggagggg gtccggcagt cccctcagcc      300
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aaaaaaaaaa cttaaaaaaaa tttttaaaaa acataaaaact actctctacc tctgctggsc      780
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<210> 102

<211> 1283

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)..(1)

<223> n equals a,t,g, or c

<400> 102

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ggccagatgc gccaggacct ggacgacatg atcggcatgc tcgatgccac cttgagctac      720
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<210> 103

<211> 2777

<212> DNA

<213> Homo sapiens

<400> 103

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gcaggtgaca tgcagcttcc agatacccac aactgtctt tctcccgccc agctcccacc      180
ccagttaatt gagatgggat tgtttctctt tctggtttct tcctaagccc ctctctcata      240
ttcctggtgt gcttatggcc tggcacacct tgtgaaacag aaaccaagc tctcatttc      300
ggagctggga tttcgattgg ctatctgcct ccctaacc aa gctgtccctt ccacctcatc      360
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aaaaaaaaa aaaaaaa 2777

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<210> 104

<211> 710

<212> DNA

<213> Homo sapiens

<400> 104

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agccaggctg agaaaacagt tactcacatt gagcagttag tgaccactag gtgggcattt 180
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ttagctgggg tgtggtggca ggcgcctgta accccagcta ctcaagaggc tgagacaaga 600
gaatcgcttg aagccaggag ttggagattg cagtgaagcca agatcatgcc acttctactcc 660
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<210> 105

<211> 1540
 <212> DNA
 <213> Homo sapiens

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 <221> misc_feature
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 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (1124)..(1124)
 <223> n equals a,t,g, or c

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 aaggtgtcag gaaggtcatg ctctctccaa agtctccaag gatgctcctt ccttgctcc 180
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<210> 106
 <211> 1428
 <212> DNA
 <213> Homo sapiens

<400> 106
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 tgggtggcaa tccaaaggaa agttatggcc gttcatcaaa aaaaataagg tactgatggg 180
 tggcgtgaaa tgagttttct aaggtgtgga gattttgact tgatctttta gtcttagaaa 240
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 aaggcagcat tactgcttta actttagaat gacttactat ttattaattt aaacagactg 720
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<210> 107

<211> 3061

<212> DNA

<213> Homo sapiens

<220>

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<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (2849)..(2849)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (2919)..(2919)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (2983)..(2983)

<223> n equals a,t,g, or c

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<221> misc_feature

<222> (2987)..(2987)

<223> n equals a,t,g, or c

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<221> misc_feature

<222> (2998)..(2998)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (3027)..(3027)

<223> n equals a,t,g, or c

<400> 107

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<211> 1691

<212> DNA

<213> Homo sapiens

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<211> 1421

<212> DNA

<213> Homo sapiens

<400> 109

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<211> 1489

<212> DNA

<213> Homo sapiens

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<210> 111
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 <212> DNA
 <213> Homo sapiens

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<211> 1477

<212> DNA

<213> Homo sapiens

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<210> 113
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<212> DNA
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<212> DNA
<213> Homo sapiens

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<223> n equals a,t,g, or c

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<220>
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<223> n equals a,t,g, or c

<400> 114

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<211> 2312

<212> DNA

<213> Homo sapiens

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<223> n equals a,t,g, or c

<400> 115

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<211> 6107

<212> DNA

<213> Homo sapiens

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<223> n equals a,t,g, or c

<400> 116

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<210> 117

<211> 767

<212> DNA

<213> Homo sapiens

<400> 117

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<210> 118

<211> 1932

<212> DNA

<213> Homo sapiens

<400> 118

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<210> 119

<211> 3436

<212> DNA

<213> Homo sapiens

<400> 119

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<210> 120

<211> 1256

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1079)..(1079)

<223> n equals a,t,g, or c

<400> 120

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<210> 121

<211> 1057

<212> DNA

<213> Homo sapiens

<400> 121

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<210> 122

<211> 2683

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (2640)..(2640)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (2676)..(2676)

<223> n equals a,t,g, or c

<400> 122

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<210> 123

<211> 3881

<212> DNA

<213> Homo sapiens

<400> 123

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<213> Homo sapiens

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<213> Homo sapiens

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<223> n equals a,t,g, or c

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<400> 133

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<211> 1564

<212> DNA

<213> Homo sapiens

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<212> DNA

<213> Homo sapiens

<400> 136

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<211> 1748

<212> DNA

<213> Homo sapiens

<400> 137

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<212> DNA

<213> Homo sapiens

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<211> 2339

<212> DNA

<213> Homo sapiens

<400> 139

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<212> DNA

<213> Homo sapiens

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<212> DNA

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<212> DNA

<213> Homo sapiens

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<211> 2207

<212> DNA

<213> Homo sapiens

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<212> DNA

<213> Homo sapiens

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<210> 147

<211> 566

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (68)..(68)

<223> n equals a,t,g, or c

<400> 147

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aagttctcct cctgatcaca gccatcttgg cagtggctgt tggtttccca gtctctcaag 180
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gccacttcct tgaagaatca aaattcctgt taataaaaga aaaacaaatg taattgaaat 480
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<210> 148

<211> 1242

<212> DNA

<213> Homo sapiens

<400> 148

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<210> 149

<211> 712

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (26)..(26)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (28)..(28)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (77)..(77)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (117)..(117)

<223> n equals a,t,g, or c

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 <223> n equals a,t,g, or c

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<400> 149
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 accnaccggt ccgaggaggt cytttaggaa gactctcaaa ggcaaatccc tgatcccccg 180
 cccaccctt agccctgccc tctcaccaga gcaaaattca ctggggactt tcccaccac 240
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 ataacttggg ctgaaatctg tttttatgag cggggccccc tgtgcctcta gtatacttgt 420
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 tgtggattag tttaactctt gtattcaacc attagtgtta ccaccttctc acattacaat 600
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<210> 150
 <211> 1200
 <212> DNA
 <213> Homo sapiens

<400> 150
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 aaggctccct gcaaaagctgg cctgtccctg gtggggctga cagcttcctt ctcaccctgc 360
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 agagtaaaga cacagctcca gagggccaca ctgtggggtc tgggcccctgc cttaggcagc 1020
 cccctcttt ggcccctcc cgtcaggccc agggcttggga gtgaaagtga ctctcagggt 1080
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 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1200

<210> 151
 <211> 1352
 <212> DNA
 <213> Homo sapiens

<400> 151
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 ttccttctgg gtggagatca tcttctgtag gaaatggaac tgcttcaagc caagaagctt 180

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tcattgctgaa	agtgaataac	agcttaaaagt	gggattctgc	tggacctgac	tcaacttttc	360
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aggagtgtga	ttgtcaataa	agtccaaggc	cagagtgcct	gctttctagt	aagtagagag	480
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<210> 152

<211> 639

<212> DNA

<213> Homo sapiens

<400> 152

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gcataccttc	tgccctatgt	gttctggaag	ctttaaagaa	ttatatattag	tgccatatatc	180
cttattctct	acatgtgtat	tgggttttta	ttttcacaa	tttctgttat	tgattatattt	240
gttttctatt	ttgctaagaa	aaattactgg	aaaattgttc	ttcacttatt	atcatttttc	300
atgtggagta	taaaatcaat	tttgtaattt	tgatagttac	aacccatgct	agaatggaaa	360
ttcctcacac	cttgcacctt	ccctactttt	ctgaattgct	atgactactc	cttgttggag	420
gaaaagtggg	acttaaaaaa	taacaaacga	ctctctcaaa	aaaattacat	taaatcacaa	480
taacagtttg	tatgccaaaa	acttgattat	ccttatgaaa	atttcaattc	tgaataaaga	540
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aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa			639

<210> 153

<211> 1434

<212> DNA

<213> Homo sapiens

<400> 153

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aaaattatga	ataggatata	ctaataaata	caaagtaata	acaaaagtca	aagcagtgtt	180
ctaaataaaa	attctgggtt	ccttaaaaaa	tattttaaat	ttatcttgaa	atagttttct	240
tagattaatc	tcaggatatg	agaaagtcaa	ttaagtgtga	gtaaagttag	tatcattaaa	300
caaattgtct	attaaatgca	mgagtggtaa	tatacagaat	ttatcaggca	ttaccaagtc	360
taggcacata	taggaaatgc	agcactcaga	atggtttcaa	tgtagtagtt	gatgcttgta	420
aggtagggga	gcttattcag	acatagtaga	tagtttctct	aatgctgtst	caattgctgg	480
cctttggcta	cctgtacttc	cscattatgg	cagcccatcc	agtcttgagt	tttcttctct	540
ggacacctta	tgctctgaaa	tcattgagcga	ggctgattca	attgggtgatt	tggttagaaa	600
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gtttttatca	tttaaaataa	gaaatataac	cttttaagct	attccacctc	ctccccagc	720
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gcttttaaat	ttgtgctctt	tttcatattt	tattcatatt	caatttatgg	tttgtaactg	1140
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ggataattta	atttacgtgc	ttctgttatt	cagaataaag	agagaagact	acgctgcata	1260
ttcaagagtt	gtaccttaac	attgggtgaaa	cattttttct	aagattttca	aaaggaatat	1320
gtgtaaatgt	agaaatcata	accactgtcc	taacttggtg	aacaaactgt	tcttaataaa	1380
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<210> 154

<211> 370

<212> DNA

<213> Homo sapiens

<400> 154

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acagcctagt	gttaacattc	ttggtatctt	tttgtgcctt	atctaaaaaca	tttctcgatc	120
actggtttca	gatgttcatt	tattatattc	ttttcaaaga	ttcagagatt	ggcttttgct	180
atccactatt	gtatgttttg	tttcattgac	ctctagtgtg	accttgatct	ttcccacttt	240
ctgttttcgg	attggagaag	atgtaccttt	tttgtcaact	cttactttta	tcagatgatc	300
aactcacgta	tttggtatctt	tatttgtttt	ctcaataaaa	tatttaaggt	taaaaaaaaaa	360
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<210> 155

<211> 2067

<212> DNA

<213> Homo sapiens

<400> 155

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tatttcagtg	gctggtarca	gtatatatgt	catgtggaag	gtggaraagg	aaatgaatac	240
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agcgtgaaac	tcctacatta	gaatatataa	agtcacttta	aatatctata	tttgtaacag	1980
aagtagtgta	cagatatattt	attacagcat	ttttgtgtaa	atgcagaatt	aaagtgaata	2040
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<210> 156

<211> 867

<212> DNA

<213> Homo sapiens

<400> 156

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ttctttctct	ccttctcact	ctctcccttc	cttcccttct	tcctttctct	ttcttttttt	180
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<210> 157

<211> 1422

<212> DNA

<213> Homo sapiens

<400> 157

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gggtcagcag	ggtgaaaccg	aaccccagaa	aacttgatga	agaaatgtct	tttgcccgtt	360
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<210> 158

<211> 1288

<212> DNA

<213> Homo sapiens

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<400> 158
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1288

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<210> 159
<211> 1152
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<222> (668)..(668)
<223> n equals a,t,g, or c

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<220>
<221> misc_feature
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<223> n equals a,t,g, or c

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<220>
<221> misc_feature
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<223> n equals a,t,g, or c

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<220>
<221> misc_feature
<222> (1088)..(1088)
<223> n equals a,t,g, or c

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<220>
<221> misc_feature
<222> (1110)..(1110)
<223> n equals a,t,g, or c

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<220>
<221> misc_feature
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<223> n equals a,t,g, or c

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<400> 159

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<210> 160

<211> 2199

<212> DNA

<213> Homo sapiens

<400> 160

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<210> 161
 <211> 1761
 <212> DNA
 <213> Homo sapiens

<220>
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 <223> n equals a,t,g, or c

<400> 161						
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<210> 162
 <211> 1999
 <212> DNA
 <213> Homo sapiens

<220>
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 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (1490)..(1490)
 <223> n equals a,t,g, or c

<400> 162

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<210> 163

<211> 1636

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (424)..(424)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (823)..(823)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (960)..(960)

<223> n equals a,t,g, or c

<400> 163

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<210> 164

<211> 1392

<212> DNA

<213> Homo sapiens

<400> 164

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cagaactaat	tatgcaagtc	ttcatttagc	tttttaaaaa	aacagcttta	ttgagttaga	720
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tatacattgt	gaaaacatca	gtcaccacaa	tcaggatact	tatttttaaaa	aacaacttta	840
tttaggatta	gtatactgat	aatgtgtcca	ttgtaagtgt	acattttcag	ttttgacaaa	900
tgtatagatt	tttgaacta	ccaccaccag	tcaagatgaa	aacgtttcta	gcactccaga	960
aagttccctt	gtgtcccttc	ttggtcagtt	attcccacca	tgctctcagg	caaccacagt	1020
tctgtctcta	tcactatata	agtgcagaaa	tttttctaca	gaatttcaca	tagatggaat	1080
catacaatat	gtactgttct	gtctggcttc	ttgaggtaag	ccaaatgtct	tttaagagtc	1140
atgcatgttt	ttgcatttat	tagtagttta	ttcttttttt	gttgggtgagt	agcattcatt	1200
gtatggatat	attccagctc	gtttttattca	ttcacttttt	ggacatttgg	gttggttatca	1260
attttgggct	cttttgaatt	aatccctccc	tccttccctc	cttcccyccc	tccctccttc	1320
cctccctccc	tcctctctc	cctccctcct	tccttccctc	cctccctccc	tccctttttt	1380
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<210> 165

<211> 717

<212> DNA

<213> Homo sapiens

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<400> 165
ggcacgagct agctgccgcc acccgaacag cctgtcctgg tgccccggct ccctgccccg      60
cgcccagtc taccctgcg cccctcactc ctcccgtcc atctgtgct gctgctgctg      120
ctcagtgcgg cgggtgtgccg gggtgaggct gggctcgaaa ccgaaagtcc cgtccggacc      180
ctccaagtgg agaccctggt ggagccccc gaaccatgtg ccgagcccg cgtttttgga      240
gacacgcttc acatacacta cacgggaagc ttggtagatg gacgtattat tgacacctcc      300
ctgaccagag accctctggt tatagaactt ggccaaaagc aggtgattcc aggtctggag      360
cagagtcttc tcgacatgtg tgtgggagag aagcgaaggg caatcattcc ttctcacttg      420
gcctatggaa aacgggggatt tccaccatct gtcccagcgg atgcagtggg gcagtatgac      480
gtggagctga ttgcactaat ccgagccaac tactggctaa agctggtgaa gggcattttg      540
cctctggtag ggatggccat ggtgccagcc ctctggggc tcattgggta tcacctatac      600
agaaaggcca atagacccaa agtctccaaa aagaagctca aggaagagaa acgaaacaag      660
agcaaaaaga aataataaat aataaatttt aaaaaactta aaaaaaaaaa aaaaaaa      717

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<210> 166

<211> 832

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (827)..(829)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (831)..(831)

<223> n equals a,t,g, or c

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<400> 166
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ctcactgagt ttacttgccc tattactatt tttttttttt aagatcttct gtctcttgtt      120
tttgttttat cccttacctg atgaaagtga acatttctag tggagaaaga agatcacagt      180
tctctaatat gggcattaag agaggggtac agctagaggg gaggtgaaaa cctgcctcca      240
ctggggtgaa aaacagtgtg ctgaggtttc agccagtgat tacactgggt aatcaaccag      300
tcccattgtt cacaaggag ttgtaatgat taacagttca ggtatgctty tgaggaaatc      360
taattgagac ctttggaaaa tagcattgtt atgaatggtg tgggtgttacg ccctggaggg      420
gaaaaggcta ggaaaaacat ttttaacttt caagtgtatt taaattaaca tccaaatgtt      480
tcagtgtgct ttactggaga ctgcctgagt ttggaattca aatattgtaa ccaaattact      540
ccaggtttct gaactaaaat gatctattga tgtttctcaa agtatagatc acagagtaag      600
aaaagaggaa atcaagtctg gtttatgaca aacttttttc catgttaaca ttggacccaa      660
agatgttamt aagagctttt tactactgtg agagraccag cgtgatgtga agacaacgaa      720
cattttaaga agtttgacta gtagacattt cgtttaagtc ttttgagggg tcttggttga      780
caaccacaaa ttttattgtg gctccccagg ctggggagaac gtggaannnc na      832

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<210> 167

<211> 734

<212> DNA

<213> Homo sapiens

<400> 167

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ggcacgagtt aaaaacgaat tgtagttggt tttcttcatt taaaatggat ctgttgagg      60
ttatgtgtgt atgttgtagt tttattgcag ccacaataat tttaccaaaag ttttcacata      120
ggcagttagc ctttacttaa tatcaagaca agtgaaaaaa tattggcatc gatgaaaccg      180
ataacattgg cctcattgga tttctttacc cattcacagt gtaaagaagt taccttcatg      240
ctttcattgt acctgcaggc ctgtgggctt gtacagtaga taattaattt ctaaaaagaa      300
cagctgcccc tttcttcct aggttaggtt atatcttcat aatcacaaga attagtgtg      360
gcaaaaataa attttgctta tgaatctttt acattgttta tatatgatta atatcatcat      420
atataatttc tgtattaagc tcatttggtt tcatttaagc tgtatactta gtcataatc      480
tttcattagt tctatggata tgagcagatc cctttactgg agcccagtat gtgctgtgtg      540
agttagaagt cattcttgct gagaagggtg ataggtaggg atttgccttg ttttgtaagt      600

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ctacaatttg ccaagagtaa ataacactgg accagctgta aaagtaaaca gtgtgtttat	660
gcattgagat actaaagcat ttaagaaaaa attaaaagat ctcttttggt taaaaaaaaa	720
aaaaaaaaaa aaaa	734

<210> 168

<211> 1209

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)..(1)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (1097)..(1097)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (1120)..(1120)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (1127)..(1127)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (1141)..(1141)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (1161)..(1161)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (1197)..(1197)

<223> n equals a,t,g, or c

<400> 168

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ccagctcggg ttccaggct cagaattttc caggagtagg ttcttgggca gtggctgtgg	120
gagctggaat ggcgagctg gaaggttact atttctcggc cgccttgagc tgtacctttt	180
tagtatcctg cctcctcttc tccgccttca gccgggcgtt gcgagagccc tacatggacg	240
agatcttcca cctgcctcag gcgcagcgct actgtgaggg ccatttctcc ctttcccagt	300
gggatcccat gattactaca ttacctggct tgtacctggg gtcaattgga gtgatcaaac	360
ctgccatttg gatctttgga tggctctgaac atgttgtctg ctccattggg atgctcagat	420
ttgttaatct tctcttcagt gttggcaact tctatttact atatttgctt ttctgcaagg	480
tacaaccag aaacaaggct gcctcaagta tccagagagt cttgtcaaca ttaacactag	540
cagtatttcc aacactttat ttttttaact tcctttatta tacagaagca ggatctatgt	600
tttttactct ttttgcgtat ttgatgtgtc tttatggaaa tcataaaact tcagccttcc	660
ttggattttg tggcttcagt ttctcgcaaa caaatatcat ctgggctgtc ttctgtgcag	720
gaaatgtcat tgcacaaaag ttaacggagg cttggaaaac tgagctacaa aagaaggaag	780
acagacttcc acctattaaa ggaccatttg cagaattcag aaaaattctt cagtttcttt	840
tggcttatcc catgtccttt aaaaacttga gtatgctttt gcttctgact tggccctaca	900
tccttctggg atttctgttt tgtgcttttg tagtagttaa tgggtgaatt gttattggcg	960

atcggagtag	tcatgaagcc	tgtcttcatt	ttcctcaact	attctacttt	ttttcattta	1020
ctctcttttt	ttcctttcct	catctcctgt	ctcctagcaa	aattaagact	tttcctttcc	1080
ttagtttggg	aaacgtngaa	ttctgttttt	tggtgggttan	cttagtnctc	tgtgggtttt	1140
nagtttggga	aattccaatt	natggctcaa	gaaatacttg	cttagcagac	caatagncca	1200
ttataattt						1209

<210> 169

<211> 2149

<212> DNA

<213> Homo sapiens

<400> 169

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tcgcgctttt	ctctccgtgc	catggcgcca	gcgaaagcca	cgaacgtggg	gcggctgcta	120
ctaggctcca	cagcgctgtg	gctttcgcag	ctcggctccg	ggacggtcgc	cgcgccaag	180
tcgggtgactg	cccacttggc	cgcgaagtgg	cccagagacc	cgctgctgct	ggaggcaagt	240
gaatttatgg	cagaagaaag	taatgaaaaa	ttttggcagt	ttttggaaac	tgtgcaagaa	300
ttagcaattt	ataagcaaac	agaatcagat	tattcttatt	acaacttaat	cctgaagaaa	360
gctggacagt	ttctagacaa	tttacacatc	aaccttttaa	agtttgcttt	ctctataagg	420
gcatactccc	cagctattca	gatgtttcag	cagattgcag	ctgatgagcc	accaccagat	480
ggttgtaatg	catttgtggg	tattcataag	aagcacacct	gtaaaattaa	tgagattaaa	540
aagctgctga	agaaagctgc	ttcaaggact	agaccttatc	tatttaaagg	agatcacaaa	600
tttctacaa	acaaagagaa	cttaccagt	gtgattctct	atgccgaaat	gggtactaga	660
acatttagtg	catttcacaa	agtattgtct	gaaaaagctc	aaaatgagga	aattctgtat	720
gttcttcgcc	attatattca	gaaaccaagc	tcacggaaaa	tgtacttata	tgggtatggg	780
gtggagctag	caattaagag	tacagaatac	aaagcactgg	atgataccca	agttaaaact	840
gtgactaata	ctactgtaga	ggatgagact	gaaacaaatg	aagttcaagg	atttctcttt	900
gggaaactaa	aagaaatata	ttcagatctt	agagataatc	tgacagcatt	ccaaaaatac	960
ctgattgaga	gtaacaaaca	aatgatgcct	ttgaaagtct	gggaactaca	agatcttagt	1020
tttcaagcag	cttctcaaat	aatgtccgct	ccagtttatg	atgccattaa	attaatgaaa	1080
gacatttcac	agaacttccc	cataaaagcc	agagtccaaa	tgattggtaa	tgtcttaatt	1140
ggatgaatat	tgtgtggagt	acttttttgc	caagaggatg	tctcgttgaa	ctgcttccat	1200
gaatactgat	gttacattaa	acatatattc	catttcaata	ggaaatacat	ttgcatagct	1260
taaagagacc	ggtgcattga	atgcaagtta	ccacgtatta	tgagaatttg	ctatataaca	1320
caactttgat	gcaattgtat	tctggttagg	gatgacagag	tataaaatta	gcaacaagta	1380
aaatatgagt	tagcttatac	taaagagata	aaatatgtga	caagtcgcag	tgcatgggca	1440
acaatggtgt	tttactgaga	ggaattggag	agcagtctac	tagcttagca	taccttcta	1500
agcatagaat	gattgctatg	cctcttattg	tcccaaacac	tattttgtac	atttattcat	1560
catacagatt	acagaatctt	caatatatgt	attctttaat	tttgaaagta	aataaatagt	1620
acatggttgg	ctacaagata	ccaaggattt	tttgggtgta	ccttgaaata	aaggagtgtg	1680
ttccttattt	acagattaa	aatgaatata	ttgatatgcc	tctttcagtc	aactttaaat	1740
gtcaagaatt	tgagaagtcg	tcatttatat	aataaaacat	gaaatatata	tgggtgtgta	1800
taaattgtcat	atctgtttag	ccataatatt	ttaattaatg	gccgttataa	aaattattag	1860
atcaaataca	aataaagtaa	aataacttta	gtcttgatca	gacagttgat	tagctctatt	1920
gatgctaagt	cagtataact	gttcagaggt	tctgatgcaa	aactctgctg	ttaatctgta	1980
attaagaaaa	aattataaaa	tatgctaaca	tgtcttaagt	gctaaattgt	aggcttgagc	2040
atatctctaa	aaccacttgg	tagacaatct	gtaaatgttt	gttgaaatga	aatatttgct	2100
aaataaatga	aaaatttgcc	ttaaaaaaa	aaaaaaaaa	aaaaaaaaa		2149

<210> 170

<211> 1084

<212> DNA

<213> Homo sapiens

<400> 170

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tgtgtgtgca	tgcatgtgtg	cgtgcatgtg	gactgttaca	ctcattgggtc	cttctgctgt	120
ctctctccct	ctcctcagcc	ctctttattc	cttgggacac	agaaattttt	aaataaggcc	180
aattaataat	cctacattgg	tctcttacgt	gttagagtga	aaagaagatt	cacatatctc	240
tcattttaaa	ttgaaagcta	gaaatgatta	agcttagtga	ggaagccatg	ttgaaagctg	300
agatagtcca	aaaactaggc	ctcttgccac	agttagccaa	gttgtgaatg	caaaagaaaa	360

gtgcctggag	gatatTTTaaa	atgctgctcc	agtgaacaca	caaacgatag	gaaagcaaaa	420
tagccttatt	gctgatatgg	agaaagtTTT	aatggTctgg	atagaagatc	aaaccaactg	480
caacatttcc	ttaagcaaaa	tcctaattca	gaacacagcc	atagctgtct	ccaattctat	540
gaagacagag	cagagaggaa	gctgtggaag	taaagtTTga	aaataagagg	ttgttcatga	600
ggtataagga	aagaagacat	ctccataaca	taaaagtgtg	agtgaacat	caagtgcgaa	660
tacagaagct	gcagcaagtt	atccagaaaa	tctaagatca	ttgaagaagg	tggctacact	720
aaacaataga	TTTTcaatat	agacaaaaga	gccttctgtt	gatttttaggc	atctagccta	780
aaatggaaga	agatgccatc	taggactTTa	atgggtagag	aggagaagtt	gatacctgtc	840
ttcaaagtaa	agactgactc	TTTTgttagg	ggctgttgca	gctggtgaca	TTaagttgaa	900
gccaatgctc	attcaccatt	ccagaaatcc	ttgtgccctt	aagaattatg	ctaaatctac	960
tctgactgtg	ttctacaagt	agaacaacaa	agcctggatg	acagcatatc	tgTTtatagt	1020
catggTTtac	taaatatTTT	aagcccactg	ttgagaccta	ctgctcagaa	aaaaaaactc	1080
gtag						1084

<210> 171

<211> 582

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (20)..(20)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (27)..(27)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (49)..(49)

<223> n equals a,t,g, or c

<400> 171

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cmcgrgtgca	tacatgccta	cctatgtata	tataaacaaa	catttttgta	aacagctcag	120
tgaggacttt	ggactggcat	aaatcatagg	aatatgatta	tgaggataca	tccaattttc	180
agattgggca	atgtatacag	tttattatca	tttctgattt	tgggtagagt	tagtactaag	240
aacagcattg	aagaaaagca	gtataacatt	aaaattaaga	agatttaaaa	tacaagagga	300
ttcataacag	tcacttttaa	aatattgttt	tggctttcta	ctttggagct	gtaattttaa	360
aaaaagaatg	aacaggTTTT	tgtatgaata	tgttagaatg	actaattata	gagcatcttt	420
caactggaat	acatgtagat	actaacacct	ggttgatttt	gatgtaattt	cagtgcatatc	480
agtgtgtgta	atctgtatta	agtgaatac	ttatgaataa	agttgtttct	gcattgcaaa	540
aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaactc	ga		582

<210> 172

<211> 1046

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (483)..(483)

<223> n equals a,t,g, or c

<400> 172

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cattcatgcg	atcagagttg	tagccaattt	ttgaaaacct	tattttcaaa	ggaaataaat	120
gattcactgt	aggattccct	taaatatcaa	gcataccag	tatatgcttt	gatggtatat	180
gtatataact	taaagttctt	tcaaaagcct	gatacagaaa	cgtgtcccca	gtttggtagc	240

aatgtggaaa	acctggctag	agatgatatg	gagctgtccc	tcagaaagca	aagccatgcc	300
tggaatccct	aataggctgc	ttagttgtga	acctgtttga	tttgccttaa	gcctctatcc	360
agaaacctgc	ccgcttccgt	ctggttaaga	agccagtggg	ggatattttc	tttgtaaca	420
ttagaatgc	aaacattccc	ttgtcaacca	agaatactca	aagctacttg	tattggaaat	480
ggncagaagg	cctaaatcca	aatttcttat	tttttataat	ttaccataga	agttttgtga	540
ttaaattctt	acttctgcca	gtggagggtt	atgcctgaaa	gtcatggggg	cctgtctgta	600
aatagacctt	aagagaagtg	cagtatttat	tctttgtagg	cataatgtgt	ttgtcactga	660
caagcattca	tattcatccc	actagtcttt	tattgcagtc	ttttattgtc	attttcagcc	720
ttatgttggg	gagctttgct	ttctcatcat	gttcacattg	tcttaagttt	tgtgagcttc	780
tgagaagag	cttggtaaag	gtttaaagg	gactttgttc	caccagggag	cattttattt	840
gggcgtctca	cccttttcta	atgaaagctg	ttgtaagcca	cctctgactt	ggaaattctg	900
aaagtatgaa	tattttttat	atcttaattg	taaaatgcca	gttctccatt	atttagatga	960
atagtagaac	actgcaccct	ttgtgcagtg	ttttgttttc	tctactgcat	tcctaccccc	1020
acccaaaaaa	aaaaaaaaaa	actcga				1046

<210> 173

<211> 558

<212> DNA

<213> Homo sapiens

<400> 173

ctgcaggaat	tcagcacgag	ytggcatgtg	acaacccagg	gctgcctgaa	aatggatacc	60
aaatcctgta	caagcgactc	tacctgccag	gagagtcctt	caccttcatg	tgctacgaag	120
gcttttagct	catgggtgaa	gtgaccatcc	gctgcatcct	gggacagcca	tcccactgga	180
acgggcccct	gcccgtgtgt	aaagtagcag	aagcggcagc	agagacgtcg	ctggaagggg	240
ggaacatggc	cctggctatc	ttcatcccgg	tcctcatcat	ctccttactg	ctgggaggag	300
cctacattta	catcacaaga	tgtcgcctact	attccaacct	ccgcctgcct	ctgatgtact	360
cccaccctta	cagccagatc	accgtggaaa	ccgagtttga	caacccattt	tacgagacag	420
gggaaaccag	agagtatgag	gtttctatct	aaagagagct	acacttgaga	aggggacttg	480
tgaactcaac	cacaatctcc	tcgagggggg	gccggtaccc	aattcgscct	atagtgaagtc	540
gtattacaat	taatgggc					558

<210> 174

<211> 685

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (678)..(679)

<223> n equals a,t,g, or c

<400> 174

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taattacatt	gtctgattta	gaatgtgatt	acattaatgc	tagatcatgt	tgctcaaaat	180
taaacaagtg	ggtaattcca	gaattgattg	gccataccat	tgtcactgta	ttactgctca	240
tgctcattgca	ctggttcac	ttccttctca	acttacctgt	tgccacttgg	aatatatatt	300
gatacattat	ggtgccgagt	ggtaacatgg	gagtgtttga	tccaacagaa	atacacaatc	360
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gcttcttcat	gtatctttat	agtatgatct	tagctttgat	aaatgactga	agctggagaa	480
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tcctccttag	aaccgtgacc	atagcagtat	atattttcct	cttggaaaca	aaaactattt	600
ttgctgtatt	tttaccatat	aaagtattta	aaaaacatga	aaaaaaaaaa	aaaaaaaaaa	660
aaaaaaaaaa	aaaaaanna	aaaaa				685

<210> 175

<211> 1669

<212> DNA

<213> Homo sapiens

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<220>
<221> misc_feature
<222> (587)..(587)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (1634)..(1634)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (1648)..(1648)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (1659)..(1659)
<223> n equals a,t,g, or c

<220>
<221> misc_feature
<222> (1668)..(1668)
<223> n equals a,t,g, or c

<400> 175
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ggcgccaggg cctgctgctt ctgcgcgtgt gcgccacagg cgcccagggg ctctacttcc      120
acatcggcga gaccgagaag cgctgtttca tcgaggaaat ccccgacgag accatggtca      180
tcggtcaggg gggctgaggg tggggaggcc ctttgtacct agctcagccc tcggcgggcg      240
tcctcctcc cgagcccagc cgggtcgctg gctccccag tacttagcct gaggggtgcc      300
cgaggacgcc agggcccctg cctagagctc cgggccgcac gtcggagggg gccgggcgga      360
gaggcgggcc actaggggcg gtcgtgacta tgtgtctgcc ccgaggcaa ctatcgtaac      420
cagatgtggg ataagcagaa ggaggtcttc ctgccctcga cccctggcct gggcatgcac      480
gtggaagtga aggaccccga cggcaagggt gtgctgtccc ggcagtacgg ctcgaggggc      540
cgcttcacgt tcacctccca cagccccggt gaccatcaa tctgtcngca ctccaattct      600
accaggatgg ctctcttcgc tgggtggcaa ctgcgkgtgc atctcgacat ccagggtggg      660
gagcatgcc acaactaccc tgagattgct gcaaaagata agctgacgga gctacagctc      720
cgcgcccgcc agttgcttga tcaggtggaa cagattcaga aggagcagga ttaccaaagg      780
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gctttctcag agtttacaac atccttacca aacagccttc tccctcctta ccacaaaaaa     1260
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tgggtactyag atgctgggct gcatcagata ggatgcacag gatcatcctg ggaagcttgt     1500
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gtatggtagg tagaataatg ggcctaccac tgtgtaaaca tatggatatg tttacctaac     1620
atgacagaag aganttaagt tgctaataag atgactgtna aataaatna                    1669

<210> 176
<211> 1038
<212> DNA
<213> Homo sapiens

<220>

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<221> misc_feature
 <222> (806)..(806)
 <223> n equals a,t,g, or c

<400> 176
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 gaggcctcgg caatattgat tttagacagg cagacttctg cgttatgacc cggctgctgg 180
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<210> 177
 <211> 921
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (4)..(4)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (9)..(9)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (11)..(11)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (15)..(15)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (20)..(20)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (901)..(901)
 <223> n equals a,t,g, or c

<400> 177
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gagcaaagtc	agcggctgcct	acagtcagca	ccatgctggg	cctgccgtgg	aagggaggtc	240
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aacccactca	caggcttgct	catgtgctgc	tcccacattc	cgtggacatc	agcactactc	720
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tgtttgagat	ctcagatcag	tgttttagaa	aatccacaca	tcttgagcct	aatcatgtag	840
tgtagatcat	taaacatcag	cattttaaga	aaaaaaaaaa	aaaaaaarct	cgaggggggg	900
nccggtaccc	agggcggaag	a				921

<210> 178

<211> 894

<212> DNA

<213> Homo sapiens

<400> 178

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tctcgtctag	aagctgcagc	ttggcctgtc	tcacctctac	acagaggggc	tgctggcgcc	120
tgacggaaaa	aggtccacac	acccgatggc	cggcccgggg	tgagcgtgc	tgctactgct	180
gctgctgctg	ctgctgctgg	gggccatggc	agggatggg	ccacagaaga	agttgaacct	240
gtcccataag	ggcatcgggg	agccatgcgg	gagacacgag	gagtggcaga	gcaactgctg	300
taccatcaac	agcctggccc	cacacacgct	ctgcaccctt	aagaccatct	tcctgcagtg	360
cctgccctgg	aggaagccca	atgggtacag	atgctgcgac	gactcagagt	gccagagcag	420
ctgctgctgc	cgcaacaaca	gcccgcagga	gttgtgcacg	ccccaaagcg	tcttcctgca	480
gtgtgtgccc	tggcgcaagc	ccaacggcga	cttctgcagc	agccatcagg	agtgtcacag	540
ccagtgtctg	atccagctga	gggagtacag	cccttcccgc	tgcatccccc	ggaccgggat	600
cctggcccag	tgccctgccc	tgtgatgtga	gctcgaacct	gggcgcgagg	gaccggcctg	660
ggccctggga	tgttcacgca	ggaccgcgtt	gcgcgggggc	tggttccagc	ggaagcttcc	720
cttacggttt	gtgctgctgt	ttctggggct	ctgaaaatct	gtgggaactg	aaaggctgtg	780
accagcctgg	tggcgcgaag	tgtctgtgag	aacaaatccc	aggcactggg	gtgtagcctg	840
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<210> 179

<211> 442

<212> DNA

<213> Homo sapiens

<400> 179

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tggaatttgc	aagaagaagt	gcaaacctga	agagatgcat	gtaaagaatg	gttgggcaat	180
gtgcggcaaa	caaagggact	gctgtgttcc	agctgacaga	cgtgctaatt	atcctgtttt	240
ctgtgtccag	acaaagacta	caagaatttc	aacagtaaca	gcaacaacag	caacaacaac	300
tttgatgatg	actactgctt	cgatgtcttc	gatggctcct	acccccgttt	ctcccactgg	360
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ttaaaaaaaa	aaaaaaaaaa	aa				442

<210> 180

<211> 582

<212> DNA

<213> Homo sapiens

<400> 180

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tcactttctc	caacaaaata	caaccttttg	gagctcaagg	agtcttgcat	ccggaaccag	180
gactgcgaga	ctggctgctg	ccaacgtgct	ccagacaatt	gcgagtcgca	ctgcgcggag	240
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tccctccttc	ttgctgcctc	ctcctcctcc	acctgctctc	ctccctaccc	agagctctgt	480
gttcaccctg	ttccccagag	cctccaccat	gagtggaggg	aagtggggag	tgattgaaat	540
aaagagcttt	ttcaatgaaa	aaaaaaaaaa	aaaaaaaaaa	aa		582

<210> 181

<211> 809

<212> DNA

<213> Homo sapiens

<400> 181

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gggcttgccc	tgactttaga	ctggaacccc	ttagtgtctc	tggtcctggg	gtggagcaga	240
tccacctacc	ccaggggaaa	tgccaactac	tttgcttca	gacctgatgc	tcctgtgggt	300
gggcctgcca	agcctgcctt	ccccagtggg	agaagagggc	cgtcttgta	aaggcctcag	360
gctgaccctt	gcagaccag	cctctgaggt	actgccagac	tggaagacc	ctcccagcca	420
cccaacagcg	tgggcccagc	ccaggacaca	tcagcccgc	actccaaatt	ctatcaagag	480
tggcattht	tctccttggt	gaggtgcggt	gtcccgggga	gctggtgcta	ttgtgcttag	540
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gaggggacag	gcccagataa	aaatcccgcc	ctattccggg	tggaatatg	tacaaggcgg	660
cggggacag	gcgggggtgg	gggcggggcg	gccggcgcc	gcagcccca	cccagggcc	720
cccgcacctc	gggcctact	tgtagaatca	gtacaaaata	ggtgctacct	aaacgttcct	780
tctacctgaa	aaaaaaaaaa	aaaaaaaaaa				809

<210> 182

<211> 1396

<212> DNA

<213> Homo sapiens

<400> 182

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agcctgcat	ggattgcttc	attacctttt	ccatacgaga	aaccacacct	tcattgtcct	420
gcacctgggtc	ttgcaaggga	tggtttatac	tgagtacacc	tggaagtat	ttggctactg	480
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tctacctgcc	tttccatgtc	atgagaggaa	gaaacaagaa	tgacaagtgt	atgactgcct	1260
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ttcaagtaga	catcaa					1396

<210> 183
 <211> 1886
 <212> DNA
 <213> Homo sapiens

<400> 183
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 taatttgtgt tccccattag catctaattt caagagcagg caaatctcat ctgttcccat 180
 ccagcccagc cagggaaacct ccagagttgc tttgcagata tgggtgtgat cctgcagaat 240
 gaggatgagc tcttcacaga tccacattct tgccttttaa aaaataaagc gggtaggcag 300
 cggggtggcg gtgtgggggtg tgtggggcaa gagctagagc gttcctcctc agtgagtttg 360
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 gagaagctga tcccagctcc caggaaatcg acacagttgc tgggtgtgtg tggtcagcac 540
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 tctgtgttca cccaagctgc ctatgcaatg acttctataa agctcagttt ttaaacacag 660
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<210> 184
 <211> 2971
 <212> DNA
 <213> Homo sapiens

<400> 184
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2971

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<210> 185

<211> 1337

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1337)..(1337)

<223> n equals a,t,g, or c

<400> 185

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gccagcgtgg cgggcctggc ggctcccggg tggtagagaga gcggtccggg aacgatgaag 180
gcctcgcagt gctgctgctg tctcagccac ctcttggctt ccgtcctcct cctgctgttg 240
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aatggcagca accctgtggc cgggcttgag acggacgatc acggagggaa ggccggggaa 480
ggctcggtgg gtggcgccct tgctgtgagc cccaacctg gcgacaagcc catgaccag 540
cgggcctga ccgtgttgat ggtggtgagc ggcgcggtgc tgggtgactt cgtggtcagg 600
acggtcagga tgagaagaag aaaccgaaag actaggagat atggagtttt ggacactaac 660
atagaaaata tggaaattgac acctttagaa caggatgatg aggatgatga caacacgtt 720
tttgatgcca atcatcctcg aagataagaa tgtgcctttt gatgaaagaa ctttatctt 780
ctacaatgaa gagtggaaatt tctatgttta aggaataaga agccactata tcaatgttgg 840

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gggggtatTT aagttacata tattttaaca acctttaatt tgctgttgca ataaataccg 900
tatcctttta ttatatcttt atatgtatag aagtactctr ttaatgggct cagagatggt 960
ggggataaag tatactgtaa taatttatct gtttgaaaat tactataaaa cgggtgttttc 1020
tgatcgggttt ttgtttcctg cttaccatat gattgtaaatt tgttttatgt attaatcagt 1080
taatgctaatt tatttttgct gatgtcatat gttaaagagc tataaatccc aacaaccaac 1140
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aaaagaagcc aaatttatta ctttgtgttg ggggttttaa aatattaaga aatgtctaag 1260
ttattgtttg caaaacaata aatatgattt taaattctct taaaaaaaaa aaaaaaaccc 1320
ccgggggggg gcccggg 1337

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<210> 186

<211> 1129

<212> DNA

<213> Homo sapiens

<400> 186

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cccagtgat cccagcctat agtggtgaaa aaaaatgctg gaacagatca gggcactgca 120
ggaaacaatg caaagatgga gaagcagtga aagatacatg caaaaatctt cgagcttgct 180
gcattccatc caatgaagac cacaggcgag ttccctgcgac atctcccaca cccttgagtg 240
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aagtaagcag caagaaagat atggttgaag agtctgaggc gggaagggga actgagacct 360
ctcttccaaa tgttcaccat agctcatgac ttctctcctg ctatcactca cccctgtcct 420
cagagtgata aactaagtca catacagata aagcactgaa aacaccacag tgaccctccc 480
acccccacc aatatgtaatt tctattaata gaaacagctg tgtaaagaag tctaaaattt 540
tactatttcc caatgataaa ctcttcagtg ctcttcttga aatgtcacat tatttcccaa 600
caagttatac ctatttttag tattcttggt gctagtgcc a tgcacaactt caatagctag 660
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gcttttatgg ctctgtagac ccattctttt gaccaagcct tgatcacaca tggacatcca 1020
agggtaatca tggaccccca attgtgggtg aaaggatgga tcatttatct acctgattac 1080
tgagagcttt atttgtctcc ctctgatagc aaaaaaaaaa aaaaaaaaaa 1129

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<210> 187

<211> 799

<212> DNA

<213> Homo sapiens

<400> 187

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ggagacgggtg ggtgaccaga gagtccctgtc taccctagga ggagaacatt cagcccaaat 60
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ttcctgggat tggcagaagc ctgtactcct cgtgaagtca acttgctgaa agggatcata 180
ggtctcatga gcagactgtc accggatgag atcctaggct tgctgagcct ccaagtactg 240
catgaagaaa caagtggctg caaggaggaa gttaaaccct tctcaggcac caccatccc 300
aggaaaccac tccccaagag gaagaacacg tggaaacttc tgaaatgcgc ctacatgggtg 360
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ttactgccac tactgtaact tggaaactgga catcagggat gatccctgct gttctttcta 480
gtgagcctgc tccatctcag cttagccttc acaaggcctc catctcccag gcattctaac 540
ctctgaagaa agctctctgt cccctggact gcctgtgtgg agggtaatga actgggtcct 600
ttaaggaatg gcacctgggt gccacagagg atggccagaa ggtgtctgtg ggggccatgc 660
cttaggggga tgcaccaggg gcggctgaga gagcaactgc agggatttcc cctaaaatct 720
ctcctccaga tcgttctcga actttcccca ctacttccat aataaaatgt atacttgttg 780
aaaaaaaaaa aaaaaaaaaa 799

```

<210> 188

<211> 1689

<212> DNA

<213> Homo sapiens


```

<400> 188
actatagaag tgcctgcag taccggctcc ggaattaagg gtcgaccac gcgtccgggc 60
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ggtaggtggg ttataaatat tgggacttaa ggcagcttgt tctatgtatt tatctttgct 180
cttgggtgac ttagggaatg attttatttg atttaacctt ctttctgttt gccccgagaa 240
tactcgccag tggcgcttgc agttgtagca tttaccccaa gataactttg cctacgaaat 300
atttcgcttt tattatttgc acatcattct agtatatgga ctttggaaac aaaagacatt 360
gttctattta tagcattctt tttttttttt tagtagcggg atttccattt acaaaatata 420
gtaactcttg attactgaaa atgtcaaadc ctagaaaacg tagcatgcct atacatgatg 480
ttaacatcat tctcgaacag ttgttggcgg aagattcatt tgatgaatcc aatttttttg 540
aaatagacaa ttctgatgtt ctctttagaa ataactcagt ttttatcttt tttcacattg 600
aaaatcagtt agatttgctt aagcctcaaa gagaatgttt atgtaaatta gcgctggcaa 660
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gtctttctga aagtgtgtgg cttgaaggga tgaataaata ttttcttaat atattcaaaa 780
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acatcaagtc attagaattt atctaagct tatcatgatt tgataagaca tccattgcat 1560
gcagctgttt tagctcagtg caaaacactg aaattgtgat tcttagactg tttctgagac 1620
atttggtatg aaataaatgt ataaatgtta aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1680
agggcggcc 1689

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<210> 189

<211> 420

<212> DNA

<213> Homo sapiens

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<400> 189
ggcacgagag agagcagagc tatacatagc tatccaggtc taacttcacg aagaatagaa 60
tggtttcttt tcattttcaa tgtacatcat actttgtcag actttttttt cagttgcagc 120
tcttcgttgg actggtgata gtattggctt tattaatctc tcattctctc acttattcat 180
tccacaaaca tttgtagaag gccaccaagc tctagggaga ggaaaatggg tttataaatt 240
agtgtcttct gggtataaag aaattttata tctgtactac ttaatagtag ccactagcca 300
catgtggttt tcgaacaaga tttccatcac ctctccaacc actttctcct cattggtcag 360
atctagacct cgagaaactg ttcctttcat tgttttctcc gccttctaca aactgagata 420

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<210> 190

<211> 1090

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (8)..(8)

<223> n equals a,t,g, or c

<220>

<221> misc_feature

<222> (28)..(28)

<223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (43)..(43)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (54)..(54)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (95)..(95)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (545)..(545)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (863)..(863)
 <223> n equals a,t,g, or c

<400> 190
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 tctatataag cagagctcgt ttagtgaacc gtcaagatcc gcctggagac gccatccacg 180
 ctgttttgac cctccataga agacaccggg accgatccag cctccggact ctagecctagg 240
 cttttgcaaa aagctattta ggtgacacta tagaaggtag gmctgcaggt accgggtccgg 300
 aattcccggg tcgaccacag cgtccgccag cctggaggcc cagacgtggc gcagcgactc 360
 ggaggttcgc ctccagcttg cgcacatctt gcggccgggt cccgatgagc ctctgttgc 420
 ctccgctggc gctgctgctg cttctcgcgg cgcttgtggs cccagccamr gccgccactg 480
 cctaccggcc ggactggaac cgtctgagcg gcctaaccgg cgcccgggta gagacctgcg 540
 ggggnatgac agctgaaccg cctaaggag agkgaaggct ttcgtcacgc aggacattcc 600
 attctatcac aamctgggtga tgaaacacct ccctggggcc gaccctgagc tcgtgctgct 660
 gggccgcgcg tacgaggaac tagagcgcat cccactcagt gaaatgaccc gcgaagagat 720
 caatgcgcta gtgcaggagc tcggcttcta ccgcaaggcg gcgcccagc gcgaggtgcc 780
 ccccgagtac gtgtgggcgc ccgcgaagcc cccagaggaa acttcggacc acgctgacct 840
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 agcgctcagc atcccgggaa tacttctctt gctgagagcc gatgcccgtc cccggggccag 960
 caggggatggg gttggggagg ttctcccaac cccactttct tccttcccca gctccactaa 1020
 attccctcct gccttaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1080
 aaaaaaaaaa 1090

<210> 191
 <211> 1676
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (798)..(798)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (927)..(927)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (944)..(944)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (974)..(974)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (1035)..(1035)
 <223> n equals a,t,g, or c

<220>
 <221> misc_feature
 <222> (1058)..(1058)
 <223> n equals a,t,g, or c

<400> 191
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 ttaccaacca ggagctgctg aggaagggtg gcagtaacaa ccaggatgtc gtctcctgtg 120
 acatggcctg caagggcctg ttgcagcagg ttcagggtcc tcggctgccc tggacgcggc 180
 tccctcctgtt gctgctgggtc ttgctgtag gcttcctgtg ccatgacctc cggtcacaca 240
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 cgtgggtttg tgacagtctc accagtctct ctcagaggct acagatccag ctccccgatt 540
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 ctgatatccc agcagtangc cctgccttcc tggccactga tttctgcatg ggtagaccat 840
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 ggggacaggg gccnagcaag catctcagcc tcctaccac aattccactg aacacttttc 1020
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 tactttctcc aactttccat tccccatcat gctgggggtc ttggtcacaa ggctcagctt 1500
 ctctccactg tccatccctc ctatcatctg tagagcagag cacaggcagt tgtgtgcctt 1560
 gggcccaggg aaccttccat caacctgaga caggactcag tatatggttc ttgggtatgc 1620
 cctaccaggt ggaataaagg acacagattt gatttctaaa aaaaaaaaaa aaaaaa 1676

<210> 192
 <211> 1569
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (341)..(341)
 <223> n equals a,t,g, or c

<400> 192

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agtgcagaga	ttacagggcat	gagccactgc	acctggcctc	aagaaaaatt	atatatcacg	120
tggaaatagga	tagtagtctc	tgactgatt	ttcgttgata	atggctgttc	ttcttatcac	180
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atttgccttc	ttgtcaaaga	aggagccaat	gttgttttaa	aatttttagct	tgagagatag	420
gtggggaaga	aattaaatag	acaagtaatc	mctattcaga	agagaaggga	gagtcattgt	480
acgaggccca	agatacttgc	ccaaaaatat	cgcagagaaa	aactagtctt	tggggctcta	540
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ctctcagttc	ttcctacaaa	cttagaaagt	ctaatactct	aatgtttact	tatgtagcaa	960
cctccctttc	tcccatccct	aaatcctctt	gtaattaatt	attttccttt	ggaacttttt	1020
aaatctacaa	tttctttata	atatggtaac	caatattaat	tttcttggtc	tgcgccaagt	1080
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aattcttgat	tgtttactgt	gttagatatt	ggggtatccc	caatacctga	cagctgtgag	1260
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taccatttga	ccaagcaatt	ctacacatag	gattcacctt	aaaaaaaaaa	aaaaaaaaaa	1560
aaactcgag						1569

<210> 193

<211> 1251

<212> DNA

<213> Homo sapiens

<400> 193

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agctcattgc	tccactggag	ggctacactc	ggagtgcgca	gatcgttttt	atcctgctca	180
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caacatctgt	aaactaggag	aactggagaa	gactccacgc	ccttcacgct	ttgggtatctg	1140
gagatttcca	gggcccctcg	ccgccacgtc	cctgactctc	gggtgatctt	ccttgtatca	1200
ataaatacag	ccgaggttgc	tgaraaaaaa	aaaaaaaaaa	aaaagtcgag	c	1251

<210> 194

<211> 1345

<212> DNA

<213> Homo sapiens

<400> 194

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tgccatggct	gtgatgaacc	acccatgtatg	ccctgtggag	aactgggcct	acaacgagtc	180
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ccccctcatc	agtggccctg	atctgcctcc	tgcgctacgg	gcagctcctg	gagcagagtc	300
ggcactcttg	ggttaacacc	acggcactca	tcacaggctg	caccaacgct	gcgggcctct	360
tgggtggttg	caactttcag	gtggatcatg	ccaggctctt	gcactacgtt	ggagctggcg	420
tggccttccc	tgcggggctg	ctctttgttt	gcctgcactg	tgctctctcc	taccaagggg	480
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gggcagccct	gtgtgagtgg	gtgtgtgtca	tcgatatcct	cattttctat	ggcaccttca	660
gctacgagtt	tggggcagtc	tcctcagaca	cactggtggc	tgactgcag	cctacccttg	720
gccgggcctg	caagtcctcc	gggagcagca	gcacctccac	ccacctcaac	tgtgcccccg	780
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cccagtgcc	aagccagacc	actggggttt	cctgctgcag	gaattggggg	ctgggaacag	1140
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tttctgggccc	cactgagctg	cactgggatt	cttcaactctg	cccctcactt	cctttagggc	1260
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<210> 195

<211> 1323

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1086)..(1087)

<223> n equals a,t,g, or c

<400> 195

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aaggcagcct	acctgtcact	tcagcactgc	ctgcactttt	ggaaaaatgga	aagacaaatg	240
gggaccaga	ttgtgaagcc	tctgtcctcg	cgctgaccct	gagctgcctg	ggaggagctt	300
agtcaggaga	ccaaggccag	gatggaggaa	gaagcctaca	gcaagggatt	ccaagaaggt	360
yttaaagaaga	ccaaagaact	tcaagacctg	aaggaggagg	aggaagaaca	gaagagttag	420
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agcaaaacttg	aagaattggg	ccatttctta	caagtcatgt	atcccaaact	gtgtcagcac	540
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<210> 196

<211> 669

<212> DNA

<213> Homo sapiens

<400> 196

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agcaatgctg	gtggcatcgt	cctgtgtaca	catgcagagc	taatacccaa	actaaaaact	180
gggtaactgg	ccctgaagtg	cttcccaatc	agtaagccac	agggaaatgt	ttgattttta	240
tgttctgttg	gattttgggt	tgcttggcat	atctaaaggt	gcctttactt	ttcttttttt	300
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agattttttt	attacagata	tgctccactg	tttttaaatg	tgaacttgtg	cgcaaatgtg	600
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<210> 197

<211> 1271

<212> DNA

<213> Homo sapiens

<400> 197

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gaaggcgcc	aagcccgag	agacccacg	gccaccagc	ctttctgggg	ctccccaaac	180
accccgctac	agccggtg	cacccaacca	cacagtgtct	agcgctcttc	tgctccctgcc	240
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<210> 198

<211> 933

<212> DNA

<213> Homo sapiens

<400> 198

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gccctggcca	ggtcctggcg	gcccatgggg	gttctgggga	gggggagggg	ggaagtcatg	180
gggggtcaga	ggtggagggt	gaagaatgag	aaagtggggg	agttaggctt	agctcaggaa	240
ccatgtgtcc	ctgcccactc	ccctccttcc	ttgccctccc	ctacctccct	gcctctacat	300
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<210> 199

<211> 470

<212> DNA

<213> Homo sapiens

<400> 199

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taataagagt tccacaatca atagaaatct atcttggcag gcacttcctt ttaccacta 180
gaattttttc ccttgggagt tcacgatccc cagaaactgt gatatgagcc attcaatatt 240
gatgtactaa aacagtgtc tgcttaata cagtttttca acatacagtc ttggaagaaa 300
caaaatccaa aataaattcc aatagtccag taacagggaat aaagacaact attgcaaatt 360
aaatcttaca gacttatatg aaagctgttg ttaacagctg ggtactagtt atttgaaaag 420
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<210> 200

<211> 1020

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (3)..(3)

<223> n equals a,t,g, or c

<400> 200

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<211> 1881

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (70)..(70)

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